

## (12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization  
International Bureau(43) International Publication Date  
19 September 2002 (19.09.2002)

PCT

(10) International Publication Number  
**WO 02/071928 A2**(51) International Patent Classification<sup>7</sup>: **A61B**

(21) International Application Number: PCT/US02/07826

(22) International Filing Date: 14 March 2002 (14.03.2002)

(25) Filing Language: English

(26) Publication Language: English

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(30) Priority Data:

60/276,025	14 March 2001 (14.03.2001)	US
60/276,026	14 March 2001 (14.03.2001)	US
60/311,732	10 August 2001 (10.08.2001)	US
60/323,580	19 September 2001 (19.09.2001)	US
60/325,149	26 September 2001 (26.09.2001)	US
60/324,967	26 September 2001 (26.09.2001)	US
60/325,102	26 September 2001 (26.09.2001)	US

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(84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— without international search report and to be republished upon receipt of that report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 02/071928 A2

(54) Title: NUCLEIC ACID MOLECULES AND PROTEINS FOR THE IDENTIFICATION, ASSESSMENT, PREVENTION, AND THERAPY OF OVARIAN CANCER

(57) Abstract: The invention relates to newly discovered nucleic acid molecules and proteins associated with ovarian cancer. Compositions, kits, and methods for detecting, characterizing, preventing, and treating human ovarian cancers are provided.

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NUCLEIC ACID MOLECULES AND PROTEINS FOR THE IDENTIFICATION,  
ASSESSMENT, PREVENTION, AND THERAPY OF  
OVARIAN CANCER

5 RELATED APPLICATIONS

The present application claims priority from U.S. provisional patent application serial no. 60/276,025, filed on March 14, 2001, which was abandoned on September 25, 2001, and from U.S. provisional patent application serial no. 60/325,149, filed on September 26, 2001. The present application also claims priority from U.S. provisional  
10 patent application serial no. 60/276,026, filed on March 14, 2001, which was abandoned on September 25, 2001, and from U.S. provisional patent application serial no. 60/324,967, filed September 26, 2001. The present application additionally claims priority from U.S. provisional patent application serial no. 60/311,732, filed August 10, 2001, which was abandoned on September 25, 2001, and from U.S. provisional patent  
15 application serial no. 60/325,102, filed September 26, 2001. The present application also claims priority from U.S. provisional patent application serial no. 60/323,580, filed September 19, 2001. All of the above applications are expressly incorporated by reference.

20 FIELD OF THE INVENTION

The field of the invention is ovarian cancer, including diagnosis, characterization, management, and therapy of ovarian cancer.

BACKGROUND OF THE INVENTION

25 Ovarian cancer is responsible for significant morbidity and mortality in populations around the world. Ovarian cancer is classified, on the basis of clinical and pathological features, in three groups, namely epithelial ovarian cancer (EOC; >90% of ovarian cancer in Western countries), germ cell tumors (*circa* 2-3% of ovarian cancer), and stromal ovarian cancer (*circa* 5% of ovarian cancer; Ozols *et al.*, 1997, *Cancer*  
30 *Principles and Practice of Oncology*, 5th ed., DeVita *et al.*, Eds. pp. 1502). Relative to EOC, germ cell tumors and stromal ovarian cancers are more easily detected and treated

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at an early stage, translating into higher/better survival rates for patients afflicted with these two types of ovarian cancer.

There are numerous types of ovarian tumors, some of which are benign, and others of which are malignant. Treatment (including non-treatment) options and predictions of patient outcome depend on accurate classification of the ovarian cancer. Ovarian cancers are named according to the type of cells from which the cancer is derived and whether the ovarian cancer is benign or malignant. Recognized histological tumor types include, for example, serous, mucinous, endometrioid, and clear cell tumors. In addition, ovarian cancers are classified according to recognized grade and stage scales.

In grade I, the tumor tissue is well differentiated. In grade II, tumor tissue is moderately well differentiated. In grade III, the tumor tissue is poorly differentiated. This grade correlates with a less favorable prognosis than grades I and II. Stage I is generally confined within the capsule surrounding one (stage IA) or both (stage IB) ovaries, although in some stage I (*i.e.* stage IC) cancers, malignant cells may be detected in ascites, in peritoneal rinse fluid, or on the surface of the ovaries. Stage II involves extension or metastasis of the tumor from one or both ovaries to other pelvic structures. In stage IIA, the tumor extends or has metastasized to the uterus, the fallopian tubes, or both. Stage IIB involves extension of the tumor to the pelvis. Stage IIC is stage IIA or IIB in which malignant cells may be detected in ascites, in peritoneal rinse fluid, or on the surface of the ovaries. In stage III, the tumor comprises at least one malignant extension to the small bowel or the omentum, has formed extrapelvic peritoneal implants of microscopic (stage IIIA) or macroscopic (< 2 centimeter diameter, stage IIIB; > 2 centimeter diameter, stage IIIC) size, or has metastasized to a retroperitoneal or inguinal lymph node (an alternate indicator of stage IIIC). In stage IV, distant (*i.e.* non-peritoneal) metastases of the tumor can be detected.

The durations of the various stages of ovarian cancer are not presently known, but are believed to be at least about a year each (Richart *et al.*, 1969, *Am. J. Obstet. Gynecol.* 105:386). Prognosis declines with increasing stage designation. For example, 5-year survival rates for patients diagnosed with stage I, II, III, and IV ovarian cancer are 80%, 57%, 25%, and 8%, respectively.

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Despite being the third most prevalent gynecological cancer, ovarian cancer is the leading cause of death among those afflicted with gynecological cancers. The disproportionate mortality of ovarian cancer is attributable to a substantial absence of symptoms among those afflicted with early-stage ovarian cancer and to difficulty

5 diagnosing ovarian cancer at an early stage. Patients afflicted with ovarian cancer most often present with non-specific complaints, such as abnormal vaginal bleeding, gastrointestinal symptoms, urinary tract symptoms, lower abdominal pain, and generalized abdominal distension. These patients rarely present with paraneoplastic symptoms or with symptoms which clearly indicate their affliction. Presently, less than

10 about 40% of patients afflicted with ovarian cancer present with stage I or stage II. Management of ovarian cancer would be significantly enhanced if the disease could be detected at an earlier stage, when treatments are much more generally efficacious.

Ovarian cancer may be diagnosed, in part, by collecting a routine medical history from a patient and by performing physical examination, x-ray examination, and

15 chemical and hematological studies on the patient. Hematological tests which may be indicative of ovarian cancer in a patient include analyses of serum levels of proteins designated CA125 and DF3 and plasma levels of lysophosphatidic acid (LPA). Palpation of the ovaries and ultrasound techniques (particularly including endovaginal ultrasound and color Doppler flow ultrasound techniques) can aid detection of ovarian

20 tumors and differentiation of ovarian cancer from benign ovarian cysts. However, a definitive diagnosis of ovarian cancer typically requires performing exploratory laparotomy of the patient.

Potential tests for the detection of ovarian cancer (*e.g.*, screening, reflex or monitoring) may be characterized by a number of factors. The "sensitivity" of an

25 assay refers to the probability that the test will yield a positive result in an individual afflicted with ovarian cancer. The "specificity" of an assay refers to the probability that the test will yield a negative result in an individual not afflicted with ovarian cancer. The "positive predictive value" (PPV) of an assay is the ratio of true positive results (*i.e.* positive assay results for patients afflicted with ovarian cancer) to all positive results

30 (*i.e.* positive assay results for patients afflicted with ovarian cancer + positive assay results for patients not afflicted with ovarian cancer). It has been estimated that in order for an assay to be an appropriate population-wide screening tool for ovarian cancer the

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assay must have a PPV of at least about 10% (Rosenthal *et al.*, 1998, *Sem. Oncol.* 25:315-325). It would thus be desirable for a screening assay for detecting ovarian cancer in patients to have a high sensitivity and a high PPV. Monitoring and reflex tests would also require appropriate specifications.

5                   Owing to the cost, limited sensitivity, and limited specificity of known methods of detecting ovarian cancer, screening is not presently performed for the general population. In addition, the need to perform laparotomy in order to diagnose ovarian cancer in patients who screen positive for indications of ovarian cancer limits the desirability of population-wide screening, such that a PPV even greater than 10%  
10    would be desirable.

                  Prior use of serum CA125 level as a diagnostic marker for ovarian cancer indicated that this method exhibited insufficient specificity for use as a general screening method. Use of a refined algorithm for interpreting CA125 levels in serial retrospective samples obtained from patients improved the specificity of the method  
15    without shifting detection of ovarian cancer to an earlier stage (Skakes, 1995, *Cancer* 76:2004). Screening for LPA to detect gynecological cancers including ovarian cancer exhibited a sensitivity of about 96% and a specificity of about 89%. However, CA125-based screening methods and LPA-based screening methods are hampered by the presence of CA125 and LPA, respectively, in the serum of patients afflicted with  
20    conditions other than ovarian cancer. For example, serum CA125 levels are known to be associated with menstruation, pregnancy, gastrointestinal and hepatic conditions such as colitis and cirrhosis, pericarditis, renal disease, and various non-ovarian malignancies. Serum LPA is known, for example, to be affected by the presence of non-ovarian gynecological malignancies. A screening method having a greater specificity for  
25    ovarian cancer than the current screening methods for CA125 and LPA could provide a population-wide screening for early stage ovarian cancer.

                  Presently greater than about 60% of ovarian cancers diagnosed in patients are stage III or stage IV cancers. Treatment at these stages is largely limited to cytoreductive surgery (when feasible) and chemotherapy, both of which aim to slow the  
30    spread and development of metastasized tumor. Substantially all late stage ovarian cancer patients currently undergo combination chemotherapy as primary treatment, usually a combination of a platinum compound and a taxane. Median survival for

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responding patients is about one year. Combination chemotherapy involving agents such as doxorubicin, cyclophosphamide, cisplatin, hexamethylmelamine, paclitaxel, and methotrexate may improve survival rates in these groups, relative to single-agent therapies. Various recently-developed chemotherapeutic agents and treatment regimens have also demonstrated usefulness for treatment of advanced ovarian cancer. For example, use of the topoisomerase I inhibitor topectan, use of amifostine to minimize chemotherapeutic side effects, and use of intraperitoneal chemotherapy for patients having peritoneally implanted tumors have demonstrated at least limited utility. Presently, however, the 5-year survival rate for patients afflicted with stage III ovarian cancer is 25%, and the survival rate for patients afflicted with stage IV ovarian cancer is 8%.

In summary, the earlier ovarian cancer is detected, the aggressiveness of therapeutic intervention and the side effects associated with therapeutic intervention are minimized. More importantly, the earlier the cancer is detected, the survival rate and quality of life of ovarian cancer patients is enhanced. Thus, a pressing need exists for methods of detecting ovarian cancer as early as possible. There also exists a need for methods of detecting recurrence of ovarian cancer as well as methods for predicting and monitoring the efficacy of treatment. There further exists a need for new therapeutic methods for treating ovarian cancer. The present invention satisfies these needs.

## SUMMARY OF THE INVENTION

The invention relates to cancer markers (hereinafter "markers" or "markers of the inventions"), which are listed in Tables 1-3. The invention provides nucleic acids and proteins that are encoded by or correspond to the markers (hereinafter "marker nucleic acids" and "marker proteins," respectively). The invention further provides antibodies, antibody derivatives and antibody fragments which bind specifically with such proteins and/or fragments of the proteins.

In one aspect, the invention relates to various diagnostic, monitoring, test and other methods related to ovarian cancer detection and therapy. In one embodiment, the invention provides a diagnostic method of assessing whether a patient has ovarian cancer or has higher than normal risk for developing ovarian cancer, comprising the steps of comparing the level of expression of a marker of the invention in a patient

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sample and the normal level of expression of the marker in a control, *e.g.*, a sample from a patient without ovarian cancer. A significantly higher level of expression of the marker in the patient sample as compared to the normal level is an indication that the patient is afflicted with ovarian cancer or has higher than normal risk for developing ovarian cancer.

In a preferred embodiment of the diagnostic method, the marker is over-expressed by at least two-fold in at least about 20% of stage I ovarian cancer patients, stage II ovarian cancer patients, stage III ovarian cancer patients, stage IV ovarian cancer patients, grade I ovarian cancer patients, grade II ovarian cancer patients, grade III ovarian cancer patients, epithelial ovarian cancer patients, stromal ovarian cancer patients, germ cell ovarian cancer patients, malignant ovarian cancer patients, benign ovarian cancer patients, serous neoplasm ovarian cancer patients, mucinous neoplasm ovarian cancer patients, endometrioid neoplasm ovarian cancer patients and/or clear cell neoplasm ovarian cancer patients.

The diagnostic methods of the present invention are particularly useful for patients with an identified pelvic mass or symptoms associated with ovarian cancer. The methods of the present invention can also be of particular use with patients having an enhanced risk of developing ovarian cancer (*e.g.*, patients having a familial history of ovarian cancer, patients identified as having a mutant oncogene, and patients at least about 50 years of age).

In a preferred diagnostic method of assessing whether a patient is afflicted with ovarian cancer (*e.g.*, new detection ("screening"), detection of recurrence, reflex testing), the method comprises comparing:

- a) the level of expression of a marker of the invention in a patient sample,
- and
- b) the normal level of expression of the marker in a control non-ovarian cancer sample.

A significantly higher level of expression of the marker in the patient sample as compared to the normal level is an indication that the patient is afflicted with ovarian cancer.

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The invention also provides diagnostic methods for assessing the efficacy of a therapy for inhibiting ovarian cancer in a patient. Such methods comprise comparing:

- 5           a) expression of a marker of the invention in a first sample obtained from the patient prior to providing at least a portion of the therapy to the patient, and
- b) expression of the marker in a second sample obtained from the patient following provision of the portion of the therapy.

10       A significantly lower level of expression of the marker in the second sample relative to that in the first sample is an indication that the therapy is efficacious for inhibiting ovarian cancer in the patient.

          It will be appreciated that in these methods the "therapy" may be any therapy for treating ovarian cancer including, but not limited to, chemotherapy, radiation therapy, surgical removal of tumor tissue, gene therapy and biologic therapy such as the  
15       administering of antibodies and chemokines. Thus, the methods of the invention may be used to evaluate a patient before, during and after therapy, for example, to evaluate the reduction in tumor burden.

          In a preferred embodiment, the diagnostic methods of the present invention are directed to therapy using a chemical or biologic agent. These methods  
20       comprise comparing:

- a) expression of a marker of the invention in a first sample obtained from the patient and maintained in the presence of the chemical or biologic agent, and
- 25       b) expression of the marker in a second sample obtained from the patient and maintained in the absence of the agent.

          A significantly lower level of expression of the marker in the first sample relative to that in the second sample is an indication that the agent is efficacious for inhibiting ovarian cancer in the patient. In one embodiment, the first and second samples can be portions of a single sample obtained from the patient or portions of pooled samples obtained  
30       from the patient.

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The invention additionally provides a monitoring method for assessing the progression of ovarian cancer in a patient, the method comprising:

- a) detecting in a patient sample at a first time point, the expression of a marker of the invention;
- 5       b) repeating step a) at a subsequent time point in time; and
- c) comparing the level of expression detected in steps a) and b), and therefrom monitoring the progression of ovarian cancer in the patient.

A significantly higher level of expression of the marker in the sample at the subsequent time point from that of the sample at the first time point is an indication that the ovarian  
10   cancer has progressed, whereas a significantly lower level of expression is an indication that the ovarian cancer has regressed.

The invention further provides a diagnostic method for determining whether ovarian cancer has metastasized or is likely to metastasize in the future, the method comprising comparing:

- 15       a) the level of expression of a marker of the invention in a patient sample, and
- b) the normal level (or non-metastatic level) of expression of the marker in a control sample.

A significantly higher level of expression in the patient sample as compared to the  
20   normal level (or non-metastatic level) is an indication that the ovarian cancer has metastasized or is likely to metastasize in the future.

The invention moreover provides a test method for selecting a composition for inhibiting ovarian cancer in a patient. This method comprises the steps of:

- 25       a) obtaining a sample comprising cancer cells from the patient;
- b) separately maintaining aliquots of the sample in the presence of a plurality of test compositions;
- c) comparing expression of a marker of the invention in each of the aliquots; and
- 30       d) selecting one of the test compositions which significantly reduces the level of expression of the marker in the aliquot containing that test

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composition, relative to the levels of expression of the marker in the presence of the other test compositions.

The invention additionally provides a test method of assessing the ovarian carcinogenic potential of a compound. This method comprises the steps of:

- 5           a) maintaining separate aliquots of ovarian cells in the presence and absence of the compound; and
- b) comparing expression of a marker of the invention in each of the aliquots.

A significantly higher level of expression of the marker in the aliquot maintained in the  
10   presence of the compound, relative to that of the aliquot maintained in the absence of the compound, is an indication that the compound possesses ovarian carcinogenic potential.

In addition, the invention further provides a method of inhibiting ovarian cancer in a patient. This method comprises the steps of:

- a) obtaining a sample comprising cancer cells from the patient;
- 15           b) separately maintaining aliquots of the sample in the presence of a plurality of compositions;
- c) comparing expression of a marker of the invention in each of the aliquots; and
- d) administering to the patient at least one of the compositions which  
20           significantly lowers the level of expression of the marker in the aliquot containing that composition, relative to the levels of expression of the marker in the presence of the other compositions.

In the aforementioned methods, the samples or patient samples comprise cells obtained from the patient. The cells may be found in an ovarian tissue sample  
25   collected, for example, by an ovarian tissue biopsy or histology section. In one embodiment, the patient sample is an ovary-associated body fluid. Such fluids include, for example, blood fluids, lymph, ascites fluids, gynecological fluids, cystic fluids, urine, and fluids collected by peritoneal rinsing. In another embodiment, the sample comprises cells obtained from the patient. In this embodiment, the cells may be found in  
30   a fluid selected from the group consisting of a fluid collected by peritoneal rinsing, a fluid collected by uterine rinsing, a uterine fluid, a uterine exudate, a pleural fluid, and an ovarian exudate. In a further embodiment, the patient sample is *in vivo*.

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According to the invention, the level of expression of a marker of the invention in a sample can be assessed, for example, by detecting the presence in the sample of:

- 5       • the corresponding marker protein or a fragment of the protein (*e.g.* by using a reagent, such as an antibody, an antibody derivative, an antibody fragment or single-chain antibody, which binds specifically with the protein or protein fragment).
- 10       • the corresponding marker nucleic acid or a fragment of the nucleic acid (*e.g.* by contacting transcribed polynucleotides obtained from the sample with a substrate having affixed thereto one or more nucleic acids having the entire or a segment of the sequence or a complement thereof)
- a metabolite which is produced directly (*i.e.*, catalyzed) or indirectly by the corresponding marker protein.

According to the invention, any of the aforementioned methods may be performed using a plurality (*e.g.* 2, 3, 5, or 10 or more) of ovarian cancer markers, including ovarian cancer markers known in the art. In such methods, the level of expression in the sample of each of a plurality of markers, at least one of which is a marker of the invention, is compared with the normal level of expression of each of the plurality of markers in samples of the same type obtained from control humans not afflicted with ovarian cancer. A significantly altered (*i.e.*, increased or decreased as specified in the above-described methods using a single marker) level of expression in the sample of one or more markers of the invention, or some combination thereof, relative to that marker's corresponding normal levels, is an indication that the patient is afflicted with ovarian cancer. For all of the aforementioned methods, the marker(s) are preferably selected such that the positive predictive value of the method is at least about 10%.

In a further aspect, the invention provides an antibody, an antibody derivative, or an antibody fragment, which binds specifically with a marker protein or a fragment of the protein. The invention also provides methods for making such antibody, antibody derivative, and antibody fragment. Such methods may comprise immunizing a mammal with a protein or peptide comprising the entirety, or a segment of 10 amino acids or more, of a marker protein, wherein the protein or peptide may be obtained from

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a cell or by chemical synthesis. The methods of the invention also encompass producing monoclonal and single-chain antibodies, which would further comprise isolating splenocytes from the immunized mammal, fusing the isolated splenocytes with an immortalized cell line to form hybridomas, and screening individual hybridomas for  
5 those that produce an antibody that binds specifically with a marker protein or a fragment of the protein.

In another aspect, the invention relates to various diagnostic and test kits. In one embodiment, the invention provides a kit for assessing whether a patient is afflicted with ovarian cancer. The kit comprises a reagent for assessing expression of a  
10 marker of the invention. In another embodiment, the invention provides a kit for assessing the suitability of a chemical or biologic agent for inhibiting an ovarian cancer in a patient. Such kit comprises a reagent for assessing expression of a marker of the invention, and may also comprise one or more of such agents. In a further embodiment, the invention provides kits for assessing the presence of ovarian cancer cells or treating  
15 ovarian cancers. Such kits comprise an antibody, an antibody derivative, or an antibody fragment, which binds specifically with a marker protein, or a fragment of the protein. Such kits may also comprise a plurality of antibodies, antibody derivatives, or antibody fragments wherein the plurality of such antibody agents binds specifically with a marker protein, or a fragment of the protein.

20 In an additional embodiment, the invention also provides a kit for assessing the presence of ovarian cancer cells, wherein the kit comprises a nucleic acid probe that binds specifically with a marker nucleic acid or a fragment of the nucleic acid. The kit may also comprise a plurality of probes, wherein each of the probes binds specifically with a marker nucleic acid, or a fragment of the nucleic acid.

25 In a further aspect, the invention relates to methods for treating a patient afflicted with ovarian cancer or at risk of developing ovarian cancer. Such methods may comprise reducing the expression and/or interfering with the biological function of a marker of the invention. In one embodiment, the method comprises providing to the patient an antisense oligonucleotide or polynucleotide complementary to a marker  
30 nucleic acid, or a segment thereof. For example, an antisense polynucleotide may be provided to the patient through the delivery of a vector that expresses an antisense polynucleotide of a marker nucleic acid or a fragment thereof. In another embodiment,

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the method comprises providing to the patient an antibody, an antibody derivative, or antibody fragment, which binds specifically with a marker protein or a fragment of the protein. In a preferred embodiment, the antibody, antibody derivative or antibody fragment binds specifically with a protein having the sequence of any of the markers  
5 listed in Table 1, or a fragment of such a protein.

It will be appreciated that the methods and kits of the present invention may also include known cancer markers including known ovarian cancer markers. It will further be appreciated that the methods and kits may be used to identify cancers other than ovarian cancer.

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#### BRIEF DESCRIPTION OF THE DRAWINGS

*Figure 1* depicts a graph which represents the results of the TaqMan® expression study.

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#### DETAILED DESCRIPTION OF THE INVENTION

The invention relates to newly discovered markers, identified in Tables 1-3, that are associated with the cancerous state of ovarian cells. It has been discovered that the higher than normal level of expression of any of these markers or combination of these markers correlates with the presence of ovarian cancer in a patient. Methods  
20 are provided for detecting the presence of ovarian cancer in a sample, the absence of ovarian cancer in a sample, the stage of an ovarian cancer, and with other characteristics of ovarian cancer that are relevant to prevention, diagnosis, characterization, and therapy of ovarian cancer in a patient. Methods of treating ovarian cancer are also provided.

Tables 1-3 list the markers of the present invention. In the Tables the  
25 markers are identified with a name ("Marker"), the name the gene is commonly known by, if applicable ("Gene Name"), the Sequence Listing identifier of the cDNA sequence of a nucleotide transcript encoded by or corresponding to the marker ("SEQ ID NO (nts)"), the Sequence Listing identifier of the amino acid sequence of a protein encoded by the nucleotide transcript ("SEQ ID NO (AAs)"), and the location of the protein  
30 coding sequence within the cDNA sequence ("CDS").

Table 1 lists all of the markers of the invention, which are over-expressed in ovarian cancer cells compared to normal (*i.e.*, non-cancerous) ovarian cells and comprises markers listed in Tables 2 and 3. Table 2 lists newly-identified nucleotide

and amino acid sequences useful as ovarian cancer markers. Table 3 lists newly-identified nucleotide sequences useful as ovarian cancer markers.

In addition to their use in ovarian cancer, it has been found that the markers of the present invention may be used in the diagnosis, characterization, management, and therapy of additional diseases. For example, OV65 (SEQ ID NOS: 305 and 306), M593 (SEQ ID NOS: 307 and 308) and M594 (SEQ ID NOS: 309 and 310), are spondin molecules, and have one or more of the following activities: (1) neural cell adhesion and (2) neurite extension and can thus be used in, for example, the diagnosis and treatment of brain and CNS related disorders. Such brain and CNS related disorders include, but are not limited to, bacterial and viral meningitis, Alzheimers Disease, cerebral toxoplasmosis, Parkinson's disease, multiple sclerosis, brain cancers (*e.g.*, metastatic carcinoma of the brain, glioblastoma, lymphoma, astrocytoma, acoustic neuroma), hydrocephalus, and encephalitis. In another example, OV65, M593 and M594 polypeptides, nucleic acids, and modulators thereof can be used to treat disorders of the brain, such as cerebral edema, hydrocephalus, brain herniations, iatrogenic disease (due to, *e.g.*, infection, toxins, or drugs), inflammations (*e.g.*, bacterial and viral meningitis, encephalitis, and cerebral toxoplasmosis), cerebrovascular diseases (*e.g.*, hypoxia, ischemia, infarction, intracranial hemorrhage, vascular malformations, and hypertensive encephalopathy), and tumors (*e.g.*, neuroglial tumors, neuronal tumors, tumors of pineal cells, meningeal tumors, primary and secondary lymphomas, intracranial tumors, and medulloblastoma), and to treat injury or trauma to the brain.

OV25 (SEQ ID NOS: 360 and 361), an HE4 protein, has one or more of the following activities: (1) sperm maturation and (2) inhibition of extracellular proteases and can thus be used in, for example, the treatment and diagnosis of diseases and disorders relating to spermatogenesis. For example, OV25 polypeptides, nucleic acids, and modulators thereof can be used to treat testicular disorders, such as unilateral testicular enlargement (*e.g.*, nontuberculous, granulomatous orchitis); inflammatory diseases resulting in testicular dysfunction (*e.g.*, gonorrhea and mumps); cryptorchidism; sperm cell disorders (*e.g.*, immotile cilia syndrome and germinal cell aplasia); acquired testicular defects (*e.g.*, viral orchitis); and tumors (*e.g.*, germ cell tumors, interstitial cell tumors, androblastoma, testicular lymphoma and adenomatoid tumors).

OV52 (SEQ ID NOS: 190 and 191), a Pump-1 proteinase, has been found to have one or more of the following activities: (1) breakdown of extracellular matrix in normal physiological processes, such as embryonic development, reproduction, and remodeling, as well as in (2) disease processes, such as arthritis, and metastasis. Hence, 5 OV52 nucleic acids, proteins, and modulators thereof can be used to modulate disorders associated with adhesion and migration of cells, *e.g.*, platelet aggregation disorders (*e.g.*, Glanzmann's thromboasthenia, which is a bleeding disorder characterized by failure of platelet aggregation in response to cell stimuli), inflammatory disorders (*e.g.*, leukocyte adhesion deficiency, which is a disorder associated with impaired migration of 10 neutrophils to sites of extravascular inflammation), connective tissue disorders, arthritis, disorders associated with abnormal tissue migration during embryo development, and tumor metastasis.

M604 (SEQ ID NOS: 48 and 49), OV10 (SEQ ID NOS: 50 and 51), and M360 (SEQ ID NOS: 52 and 53), are Claudin molecules which have one or more of the 15 following activities: (1) it elicits fluid accumulation in the intestinal tract by altering the membrane permeability of intestinal epithelial cells and (2) thus acts as the causative agent of diarrhea. The polypeptides, nucleic acids, and modulators thereof can be used to treat colonic disorders, such as congenital anomalies (*e.g.*, megacolon and imperforate anus), idiopathic disorders (*e.g.*, diverticular disease and melanos coli), vascular 20 lesions (*e.g.*, ischemic colitis, hemorrhoids, angiodysplasia), inflammatory diseases (*e.g.*, colitis (*e.g.*, idiopathic ulcerative colitis, pseudomembranous colitis), and lymphopathia venereum), Crohn's disease, and tumors (*e.g.*, hyperplastic polyps, adenomatous polyps, bronchogenic cancer, colonic carcinoma, squamous cell carcinoma, adenoacanthomas, sarcomas, lymphomas, argentaffinomas, carcinoids, and 25 melanocarcinomas).

OV48 (SEQ ID NOS: 226 and 227), OV49 (SEQ ID NOS: 228 and 229) and OV50 (SEQ ID NOS: 230 and 231), markers for an osteopontin protein, have one or more of the following activities: (1) they act as a vessel extracellular matrix protein involved in calcification and (2) atherosclerosis. Hence, OV48, OV49 and OV50 30 nucleic acids, proteins, and modulators thereof can be used to treat heart disorders, *e.g.*, ischemic heart disease, atherosclerosis, hypertension, angina pectoris, Hypertrophic Cardiomyopathy, and congenital heart disease. They can also be used to treat

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cardiovascular disorders, such as ischemic heart disease (*e.g.*, angina pectoris, myocardial infarction, and chronic ischemic heart disease), hypertensive heart disease, pulmonary heart disease, valvular heart disease (*e.g.*, rheumatic fever and rheumatic heart disease, endocarditis, mitral valve prolapse, and aortic valve stenosis), congenital  
5 heart disease (*e.g.*, valvular and vascular obstructive lesions, atrial or ventricular septal defect, and patent ductus arteriosus), or myocardial disease (*e.g.*, myocarditis, congestive cardiomyopathy, and hypertrophic cardiomyopathy).

OV37 (SEQ ID NOS: 176 and 177), a lipocalin marker, is known to be a component of the neutrophil gelatinase complex. OV37 nucleic acids, proteins, and  
10 modulators thereof can be used to modulate the proliferation, differentiation, and/or function of leukocytes. Thus, OV37 nucleic acids, proteins, and modulators thereof can be used to treat bone marrow, blood, and hematopoietic associated diseases and disorders, *e.g.*, acute myeloid leukemia, hemophilia, leukemia, anemia (*e.g.*, sickle cell anemia), and thalassemia. OV37 polypeptides, nucleic acids, and modulators thereof can  
15 be used to treat leukocytic disorders, such as leukopenias (*e.g.*, neutropenia, monocytopenia, lymphopenia, and granulocytopenia), leukocytosis (*e.g.*, granulocytosis, lymphocytosis, eosinophilia, monocytosis, acute and chronic lymphadenitis), malignant lymphomas (*e.g.*, Non-Hodgkin's lymphomas, Hodgkin's lymphomas, leukemias, agnogenic myeloid metaplasia, multiple myeloma, plasmacytoma, Waldenstrom's  
20 macroglobulinemia, heavy-chain disease, monoclonal gammopathy, histiocytoses, eosinophilic granuloma, and angioimmunoblastic lymphadenopathy).

OV2 (SEQ ID NOS: 285 and 286), is known to be a protease inhibitor, which is associated with emphysema and liver disease. Hence OV2 polypeptides, nucleic acids, and modulators thereof can be used to diagnose and treat pulmonary  
25 (lung) disorders, such as atelectasis, cystic fibrosis, rheumatoid lung disease, pulmonary congestion or edema, chronic obstructive airway disease (*e.g.*, emphysema, chronic bronchitis, bronchial asthma, and bronchiectasis), diffuse interstitial diseases (*e.g.*, sarcoidosis, pneumoconiosis, hypersensitivity pneumonitis, bronchiolitis, Goodpasture's syndrome, idiopathic pulmonary fibrosis, idiopathic pulmonary hemosiderosis,  
30 pulmonary alveolar proteinosis, desquamative interstitial pneumonitis, chronic interstitial pneumonia, fibrosing alveolitis, hamman-rich syndrome, pulmonary eosinophilia, diffuse interstitial fibrosis, Wegener's granulomatosis, lymphomatoid

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granulomatosis, and lipid pneumonia), or tumors (*e.g.*, bronchogenic carcinoma, bronchioloalveolar carcinoma, bronchial carcinoid, hamartoma, and mesenchymal tumors). In another example, OV2 polypeptides, nucleic acids, and modulators thereof can be used to diagnose and treat hepatic (liver) disorders, such as jaundice, hepatic failure, hereditary hyperbilirubinemias (*e.g.*, Gilbert's syndrome, Crigler-Najjar syndromes and Dubin-Johnson and Rotor's syndromes), hepatic circulatory disorders (*e.g.*, hepatic vein thrombosis and portal vein obstruction and thrombosis), hepatitis (*e.g.*, chronic active hepatitis, acute viral hepatitis, and toxic and drug-induced hepatitis), cirrhosis (*e.g.*, alcoholic cirrhosis, biliary cirrhosis, and hemochromatosis), or malignant tumors (*e.g.*, primary carcinoma, hepatoma, hepatoblastoma, liver cysts, and angiosarcoma).

OV32 (SEQ ID NOS: 166 and 167) and OV33 (SEQ ID NOS: 168 and 169), kallikrein markers, are useful in detection of primary mammary carcinomas, as well as primary ovarian cancers. Hence, OV32 and OV33 polypeptides, nucleic acids, and modulators thereof can be used to diagnose and treat ovarian disorders, such as ovarian endometriosis, non-neoplastic cysts (*e.g.*, follicular and luteal cysts and polycystic ovaries) and tumors (*e.g.*, carcinomas, tumors of surface epithelium, germ cell tumors, ovarian fibroma, sex cord-stromal tumors, and ovarian cancers (*e.g.*, metastatic carcinomas, and ovarian teratoma)).

OV68 (SEQ ID NOS: 192 and 193), OV69 (SEQ ID NOS: 194 and 195), OV70 (SEQ ID NOS: 196 and 197), OV71 (SEQ ID NOS: 198 and 199), OV72 (SEQ ID NOS: 200 and 201), OV41 (SEQ ID NOS: 202 and 203), OV42 (SEQ ID NOS: 204 and 205), OV43 (SEQ ID NOS: 206 and 205), OV44 (SEQ ID NOS: 207 and 208) and OV83 (SEQ ID NOS: 209 and 210), are all mesothelin markers, and have been found to play a role in cellular adhesion. The nucleic acids, proteins, and modulators thereof can be used to diagnose, treat and modulate disorders associated with adhesion and migration of cells, *e.g.*, platelet aggregation disorders (*e.g.*, Glanzmann's thrombasthenia, which is a bleeding disorder characterized by failure of platelet aggregation in response to cell stimuli), inflammatory disorders (*e.g.*, leukocyte adhesion deficiency, which is a disorder associated with impaired migration of neutrophils to sites of extravascular inflammation), disorders associated with abnormal tissue migration during embryo development, and tumor metastasis.

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OV17 (SEQ ID NOS: 110 and 111), OV18 (SEQ ID NOS: 112 and 111), OV19 (SEQ ID NOS: 113 and 111), OV20 (SEQ ID NOS: 114 and 111), OV21 (SEQ ID NOS: 115 and 111) and OV22 (SEQ ID NOS: 116 and 117) are folate receptors, which are known to be markers of ovarian cancer. The nucleic acids, proteins, and modulators thereof can be used to diagnose, treat and modulate ovarian disorders (*e.g.*, ovarian cyst, ovarian fibroma, ovarian endometriosis, ovarian teratoma). Although these markers have been previously associated with ovarian cancer, the expression of such markers has not yet been identified in combination with the expression of other markers including those of the present invention. Such combination of markers will provide improved methods of diagnosing, characterizing, managing and treating ovarian cancer.

OV66 (SEQ ID NOS: 54 and 55), OV7 (SEQ ID NOS: 56 and 57), OV8 (SEQ ID NOS: 58 and 59) and OV81 (SEQ ID NOS: 60 and 61) are ceruloplasmin markers, known to encode a plasma metalloprotein that binds copper in the plasma. The nucleic acids, proteins, and modulators thereof can be used to diagnose, treat and modulate disorders in blood haemostasis and diseases caused by such an imbalance *e.g.*, (1) cardiovascular diseases or disorders, such as ischemic heart disease (*e.g.*, angina pectoris, myocardial infarction, and chronic ischemic heart disease), hypertensive heart disease, pulmonary heart disease, valvular heart disease (*e.g.*, rheumatic fever and rheumatic heart disease, endocarditis, mitral valve prolapse, and aortic valve stenosis), congenital heart disease (*e.g.*, valvular and vascular obstructive lesions, atrial or ventricular septal defect, and patent ductus arteriosus), or myocardial disease (*e.g.*, myocarditis, congestive cardiomyopathy, and hypertrophic cardiomyopathy); (2) neuronal diseases such as Alzheimers Disease, cerebral toxoplasmosis, Parkinson's disease, multiple sclerosis, brain cancers (*e.g.*, metastatic carcinoma of the brain, glioblastoma, lymphoma, astrocytoma, acoustic neuroma), hydrocephalus, and encephalitis; and (3) Wilson's Disease.

**TABLE 1**

Marker	Gene Name	SEQ ID NO (nts)	SEQ ID NO (AAs)	CDS
OV1	ABCB1: ATP-binding cassette, sub-family B (MDR/TAP), member 1	1	2	425..4264
M430	ADPRT: ADP-ribosyltransferase	3	4	160..3204
M571	ANXA2: annexin A2, variant 1	5	6	134..1153
M572	ANXA2: annexin A2, variant 2	7	8	50..1069
M573	ANXA4: annexin A4	9	10	74..1039
OV3	AQP5: aquaporin 5	11	12	519..1316
M352	ARHGAP8: Rho GTPase activating protein 8, variant 1	13	14	142..1536
M353	ARHGAP8: Rho GTPase activating protein 8, variant 2	15	16	1..2043
M354	ARHGAP8: Rho GTPase activating protein 8, variant 3	17	18	1..2256
M608	ARHGAP8: Rho GTPase activating protein 8, variant 4	17	19	1..2157
M355	ARHGAP8: Rho GTPase activating protein 8, variant 5	20	21	<1..1314
M356	ARHGAP8: Rho GTPase activating protein 8, variant 6	22	23	1..1902
M357	ARHGAP8: Rho GTPase activating protein 8, variant 7	24	25	<1..1281
M358	ARHGAP8: Rho GTPase activating protein 8, variant 8	26	27	1..1386
M359	ARHGAP8: Rho GTPase activating protein 8, variant 9	28	29	<1..1059
OV5	BICD1: Bicaudal D homolog 1 (Drosophila)	30	31	82..3009
M431	BTG2: BTG family, member 2	32	33	72..548
M432	CADPS: Ca <sup>2+</sup> -dependent activator protein for secretion	34	35	240..4412
M609	CDH1: cadherin 1, type 1, E-cadherin (epithelial)	36	37	125..2773
M433	CDH6: cadherin 6, type 2, K-cadherin	38	39	327..2699
M434	CDKN2A: cyclin-dependent kinase inhibitor 2A	40	41	41..511
OV9	CGN: cingulin	42	43	152..3763
OV6	CHI3L1: cartilage glycoprotein-39	44	45	127..1278
M435	CKMT1: creatine kinase, mitochondrial 1 (ubiquitous)	46	47	164..1417
M604	CLDN10: claudin 10	48	49	36..772
OV10	CLDN16: claudin 16	50	51	69..986
M360	CLDN4: claudin 4	52	53	183..812
OV66	CP: ceruloplasmin (ferroxidase), variant 1	54	55	1..3210
OV7	CP: ceruloplasmin (ferroxidase), variant 2	56	57	<1..2561
OV8	CP: ceruloplasmin (ferroxidase), variant 3	58	59	1..3198
OV81	CP: ceruloplasmin (ferroxidase), variant 4	60	61	76..3348
M103	CRABP2: cellular retinoic acid-binding protein 2	62	63	138..554

OV40	DD96: Epithelial protein up-regulated in carcinoma, membrane associated protein 17	64	65	202..546
OV4	DEC2: basic helix-loop-helix protein	66	67	135..1583
M575	dehydrogenase	68	69	339..1364
M436	DLX5: distal-less homeo box 5	70	71	204..1073
OV12	EAB1: Eab1 protein	72	73	<1..1305
OV13	ESX protein	74	75	96..1211
OV67	EVI-1: Evi-1 protein, variant 1	76	77	250..2406
OV14	EVI-1: Evi-1 protein, variant 2	78	79	250..3405
OV15	EVI-1: Evi-1 protein, variant 3	80	81	250..2433
OV16	EVI-1: Evi-1 protein, variant 4	82	83	250..3378
M437	FLJ10546: hypothetical protein FLJ10546	84	85	28..1815
OV28	FLJ12799: hypothetical protein FLJ12799	86	87	39..797
M576	FLJ13710: hypothetical protein FLJ13710	88	89	96..1712
M438	FLJ13782: hypothetical protein FLJ13782	90	91	13..1890
OV29	FLJ20150: hypothetical protein FLJ20150	92	93	78..983
M439	FLJ20327: hypothetical protein FLJ20327	94	95	306..2186
M440	FLJ20758: hypothetical protein FLJ20758, variant 1	96	97	<2..1270
M441	FLJ20758: hypothetical protein FLJ20758, variant 2	98	99	<2..2095
M442	FLJ20758: hypothetical protein FLJ20758, variant 3	100	101	465..1307
M443	FLJ22252: likely ortholog of mouse SRY-box containing gene 17	102	103	205..1449
M444	FLJ22316: hypothetical protein FLJ22316	104	105	508..1206
M400	FLJ22418: hypothetical protein FLJ22418	106	107	71..919
M445	FLJ23499: hypothetical protein FLJ23499	108	109	21..473
OV17	FOLR1: folate receptor 1 (alpha), variant 1	110	111	139..912
OV18	FOLR1: folate receptor 1 (alpha), variant 2	112	111	211..984
OV19	FOLR1: folate receptor 1 (alpha), variant 3	113	111	46..819
OV20	FOLR1: folate receptor 1 (alpha), variant 4	114	111	437..1210
OV21	FOLR1: folate receptor 1 (alpha), variant 5	115	111	11..784
OV22	FOLR3: folate receptor 3 (gamma)	116	117	57..788
OV23	GPR39: G protein-coupled receptor 39	118	119	1..1362
M446	GPRC5B: G protein-coupled receptor, family C, group 5, member B	120	121	109..1320
OV24	G-protein coupled receptor	122	123	274..1236
M447	GRB7: growth factor receptor-bound protein 7	124	125	220..1818
OV11	HAIK1: type I intermediate filament cytokeratin	126	127	61..1329
M448	HOXB7: homeo box B7	128	129	100..753
M138	HSECP1: secretory protein, variant 1	130	131	27..863
M449	HSECP1: secretory protein, variant 2	132	133	136..768
M450	HSECP1: secretory protein, variant 3	134	135	202..933
M451	HSNFRK: HSNFRK protein	136	137	642..2939
OV26	hypothetical protein (1)	138	139	<1..1140
OV27	hypothetical protein (2)	140	141	242..1483
OV31	IFI30: interferon, gamma-inducible protein 30	142	143	41..952
OV58	IGF2: somatomedin A	144	145	553..1095

M452	IMP-2: IGF-II mRNA-binding protein 2	146	147	436..2106
M453	INDO: indoleamine-pyrrole 2, 3 dioxygenase	148	149	23..1234
OV73	IPT: tRNA isopentenylpyrophosphate transferase, variant 1	150	151	15..1418
M610	IPT: tRNA isopentenylpyrophosphate transferase, variant 2	152	153	15..1418
M454	ITGA3: integrin, alpha 3	154	155	74..3274
OV30	ITGB8: integrin, beta 8	156	157	681..2990
OV34	KIAA0762: KIAA0762 protein	158	159	<1..1875
M455	KIAA0869: KIAA0869 protein	160	161	<1..2668
OV35	KIAA1154: KIAA1154 protein	162	163	<1..677
OV36	KIAA1456: KIAA1456 protein	164	165	<366..1631
OV32	KLK10: kallikrein 10	166	167	82..912
OV33	KLK6: kallikrein 6	168	169	246..980
M456	KRT7: keratin 7, variant 1	170	171	57..1466
M611	KRT7: keratin 7, variant 2	172	173	54..1463
OV53	LC27: Putative integral membrane transporter	174	175	204..1055
OV37	LCN2: Lipocalin 2 (oncogene 24p3)	176	177	1..597
M457	LEFTB: left-right determination, factor B	178	179	71..1171
M559	LPHB: lipophilin B (uteroglobin family member), prostatein-like	180	181	64..336
OV38	LYST-interacting protein LIP6	182	183	11..586
OV39	MEIS1: MEIS1 protein	184	185	66..1238
M458	MGB2: mammaglobin 2	186	187	65..352
M459	MGC3184: similar to sialyltransferase 7 ((alpha-N-acetylneuraminy) 2, 3-betagalactosyl-1, 3)-N-acetyl galactosaminide alpha-2, 6-sialyltransferase) E	188	189	176..1186
OV52	MMP7: Matrix metalloproteinase 7 (matrilysin, uterine)	190	191	28..831
OV68	MSLN: mesothelin, variant 1	192	193	88..2196
OV69	MSLN: mesothelin, variant 2	194	195	88..1980
OV70	MSLN: mesothelin, variant 3	196	197	88..1950
OV71	MSLN: mesothelin, variant 4	198	199	88..2172
OV72	MSLN: mesothelin, variant 5	200	201	88..1926
OV41	MSLN: mesothelin, variant 6	202	203	<1..>1195
OV42	MSLN: mesothelin, variant 7	204	205	85..1953
OV43	MSLN: mesothelin, variant 8	206	205	88..1956
OV44	MSLN: mesothelin, variant 9	207	208	89..1975
OV83	MSLN: mesothelin, variant 10	209	210	295..2187
OV45	MUC1: mucin 1	211	212	58..1605
M460	MUC16: mucin 16, variant 1	213	214	<1..5352
M461	MUC16: mucin 16, variant 2	215	216	25..3471
M612	MUC16: mucin 16, variant 3	215	217	<1..5673
M462	MYOM2: myomesin (M-protein)	218	219	49..4446
M463	NaPi-lib: sodium dependent phosphate transporter isoform	220	221	36..2105
M464	NME5: protein expressed in non-metastatic cells 5	222	223	15..653

OV47	NUFIP1: nuclear fragile X mental retardation protein interacting protein 1	224	225	1..1488
OV48	OPN-a: Secreted phosphoprotein-1 (osteopontin, bone sialoprotein)	226	227	1..942
OV49	OPN-b: Secreted phosphoprotein-1 (osteopontin, bone sialoprotein)	228	229	88..990
OV50	OPN-c: Secreted phosphoprotein-1 (osteopontin, bone sialoprotein)	230	231	1..861
M578	PAEP: progesterone-associated endometrial protein, variant 1	232	233	36..578
M579	PAEP: progesterone-associated endometrial protein, variant 2	234	233	36..578
M580	PAEP: progesterone-associated endometrial protein, variant 3	235	233	36..578
M581	PAEP: progesterone-associated endometrial protein, variant 4	236	233	36..578
M583	PAEP: progesterone-associated endometrial protein, variant 5	237	238	45..305
M582	PAEP: progesterone-associated endometrial protein, variant 6	239	240	45..521
M613	PAEP: progesterone-associated endometrial protein, variant 7	239	241	45..521
M465	PAX8: paired box gene 8, isoform 8A	242	243	11..1363
M466	PAX8: paired box gene 8, isoform 8B, variant 1	244	245	11..1174
M614	PAX8: paired box gene 8, isoform 8B, variant 2	244	246	11..1174
M467	PAX8: paired box gene 8, isoform 8C	247	248	161..1357
M468	PAX8: paired box gene 8, isoform 8D	249	250	161..1126
M469	PAX8: paired box gene 8, isoform 8E	251	252	161..1024
M470	PRAME: preferentially expressed antigen in melanoma	253	254	236..1765
M615	PRKCI: protein kinase C, iota	255	256	205..1968
M605	PRP4: serine/threonine-protein kinase PRP4 homolog, variant 1	257	258	<1..3133
M606	PRP4: serine/threonine-protein kinase PRP4 homolog, variant 2	259	258	<1..3133
M607	PRP4: serine/threonine-protein kinase PRP4 homolog, variant 3	260	258	<1..3133
OV80	PRSS8: prostatic	261	262	229..1260
OV51	PTGS1: prostaglandin-endoperoxide synthase 1	263	264	6..1805
M312	PTK9: protein tyrosine kinase 9	265	266	61..1113
OV54	pyruvate dehydrogenase complex component E2	267	268	49..>358
OV55	S100A1: S100 calcium-binding protein A1	269	270	114..398
M471	S100A11: S100 calcium-binding protein A11 (calgizzarin)	271	272	121..438
M68	S100A2: S100 calcium-binding protein A2	273	274	41..334
M585	S100A6: S100 calcium-binding protein A6 (calcyclin)	275	276	103..375

OV57	SCNN1A: sodium channel, nonvoltage-gated 1 alpha, variant 1	277	278	100..2109
OV85	SCNN1A: sodium channel, nonvoltage-gated 1 alpha, variant 2	279	280	96..2105
M472	secreted protein (HETKL27)	281	282	88..618
M473	SEMA3A: sema domain, immunoglobulin domain (Ig), short basic domain, secreted, (semaphorin) 3A	283	284	16..2331
OV2	SERPINA1: alpha-1 antitrypsin	285	286	35..1291
M474	Similar to hypothetical protein, MGC: 7199	287	288	173..1053
M586	Similar to proteasome (prosome, macropain) subunit, alpha type, 3	289	290	45..791
M587	Similar to zinc finger protein 136	291	292	139..1524
M475	SLPI: secretory leukocyte protease inhibitor (antileukoproteinase), variant 1	293	294	271..447
M185	SLPI: secretory leukocyte protease inhibitor (antileukoproteinase), variant 2	295	296	19..417
OV60	SNCG: synuclein, gamma	297	298	49..432
OV59	SORL1: sortilin-related receptor	299	300	198..6842
OV56	SPINT2: serine protease inhibitor, Kunitz type, 2, variant 1	301	302	301..1059
OV84	SPINT2: serine protease inhibitor, Kunitz type, 2, variant 2	303	304	332..919
OV65	SPON1: VSGP/F-spondin, variant 1	305	306	25..2448
M593	SPON1: VSGP/F-spondin, variant 2	307	308	180..2984
M594	SPON1: VSGP/F-spondin, variant 3	309	310	180..2687
OV82	ST14: matriptase	311	312	209..2557
M476	TACSTD2: tumor-associated calcium signal transducer 2	313	314	616..1587
M588	TFPI2: tissue factor pathway inhibitor 2	315	316	57..764
OV86	TMPRSS4: transmembrane protease, serine 4	317	318	310..1623
OV74	TPH: tryptophan hydroxylase, variant 1	319	320	1..1335
OV75	TPH: tryptophan hydroxylase, variant 2	321	322	1..1401
M327	TSPAN-1: Tetraspan NET-1 protein, variant 1	323	324	124..900
M328	TSPAN-1: Tetraspan NET-1 protein, variant 2	325	326	1..726
OV46	TTID: myotilin	327	328	281..1777
M589	UCH2: Ubiquitin carboxyl-terminal hydrolases family 2	329	330	551..2940
OV63	unnamed gene (1)	331	332	71..919
OV64	unnamed gene (2)	333	334	28..804
OV76	unnamed gene (3)	335	336	69..773
OV77	unnamed gene (4)	337	338	223..1284
OV78	unnamed gene (5), variant 1	339	340	84..2450
M616	unnamed gene (5), variant 2	341	342	84..2450
OV79	unnamed gene (6)	343	344	69..392
OV87	unnamed gene (7)	345	346	509..2428
OV88	unnamed gene (8)	347	348	71..919
M477	unnamed gene (9), variant 1	349	350	246..992
M617	unnamed gene (9), variant 2	349	351	246..992
M478	unnamed gene (9), variant 3	352	353	246..1004

M479	unnamed gene (9), variant 4	354	355	246..1049
M590	unnamed gene (10), variant 1	356	357	21..404
M591	unnamed gene (10), variant 2	358	357	21..404
M592	unnamed gene (10), variant 3	359	357	21..404
OV25	WFDC2: Epididymis-specific, whey-acidic protein type, four-disulfide core; putative ovarian carcinoma marker	360	361	28..405
M480	XRCC5, KU80: ATP-dependant DNA helicase II	362	363	34..2232

**TABLE 2**

Marker	Gene Name	SEQ ID NO (nts)	SEQ ID NO (AAs)	CDS
M354	ARHGAP8: Rho GTPase activating protein 8, variant 3	17	18	1..2256
M608	ARHGAP8: Rho GTPase activating protein 8, variant 4	17	19	1..2157
M355	ARHGAP8: Rho GTPase activating protein 8, variant 5	20	21	<1..1314
M356	ARHGAP8: Rho GTPase activating protein 8, variant 6	22	23	1..1902
M357	ARHGAP8: Rho GTPase activating protein 8, variant 7	24	25	<1..1281
M358	ARHGAP8: Rho GTPase activating protein 8, variant 8	26	27	1..1386
M359	ARHGAP8: Rho GTPase activating protein 8, variant 9	28	29	<1..1059
OV66	CP: ceruloplasmin (ferroxidase), variant 1	54	55	1..3210
OV81	CP: ceruloplasmin (ferroxidase), variant 4	60	61	76..3348
M575	dehydrogenase	68	69	339..1364
OV67	EVI-1: Evi-1 protein, variant 1	76	77	250..2406
M440	FLJ20758: hypothetical protein FLJ20758, variant 1	96	97	<2..1270
M441	FLJ20758: hypothetical protein FLJ20758, variant 2	98	99	<2..2095
M449	HSECP1: secretory protein, variant 2	132	133	136..768
M450	HSECP1: secretory protein, variant 3	134	135	202..933
OV73	IPT: tRNA isopentenylpyrophosphate transferase, variant 1	150	151	15..1418
M610	IPT: tRNA isopentenylpyrophosphate transferase, variant 2	152	153	15..1418
M611	KRT7: keratin 7, variant 2	172	173	54..1463
OV68	MSLN: mesothelin, variant 1	192	193	88..2196
OV69	MSLN: mesothelin, variant 2	194	195	88..1980
OV70	MSLN: mesothelin, variant 3	196	197	88..1950
OV71	MSLN: mesothelin, variant 4	198	199	88..2172
OV72	MSLN: mesothelin, variant 5	200	201	88..1926
OV83	MSLN: mesothelin, variant 10	209	210	295..2187
M460	MUC16: mucin 16, variant 1	213	214	<1..5352
M583	PAEP: progestagen-associated endometrial protein, variant 5	237	238	45..305

M613	PAEP: progesterone-associated endometrial protein, variant 7	239	241	45..521
M614	PAX8: paired box gene 8, isoform 8B, variant 2	244	246	11..1174
M605	PRP4: serine/threonine-protein kinase PRP4 homolog, variant 1	257	258	<1..3133
M606	PRP4: serine/threonine-protein kinase PRP4 homolog, variant 2	259	258	<1..3133
M607	PRP4: serine/threonine-protein kinase PRP4 homolog, variant 3	260	258	<1..3133
OV85	SCNN1A: sodium channel, nonvoltage-gated 1 alpha, variant 2	279	280	96..2105
M475	SLPI: secretory leukocyte protease inhibitor (antileukoproteinase), variant 1	293	294	271..447
OV84	SPINT2: serine protease inhibitor, Kunitz type, 2, variant 2	303	304	332..919
M593	SPON1: VSGP/F-spondin, variant 2	307	308	180..2984
M594	SPON1: VSGP/F-spondin, variant 3	309	310	180..2687
OV82	ST14: matriptase	311	312	209..2557
OV86	TMPRSS4: transmembrane protease, serine 4	317	318	310..1623
OV74	TPH: tryptophan hydroxylase, variant 1	319	320	1..1335
OV75	TPH: tryptophan hydroxylase, variant 2	321	322	1..1401
M327	TSPAN-1: Tetraspan NET-1 protein, variant 1	323	324	124..900
M589	UCH2: Ubiquitin carboxyl-terminal hydrolases family 2	329	330	551..2940
OV76	unnamed gene (3)	335	336	69..773
OV77	unnamed gene (4)	337	338	223..1284
OV78	unnamed gene (5), variant 1	339	340	84..2450
M616	unnamed gene (5), variant 2	341	342	84..2450
OV79	unnamed gene (6)	343	344	69..392
OV87	unnamed gene (7)	345	346	509..2428
OV88	unnamed gene (8)	347	348	71..919
M477	unnamed gene (9), variant 1	349	350	246..992
M617	unnamed gene (9), variant 2	349	351	246..992
M478	unnamed gene (9), variant 3	352	353	246..1004
M479	unnamed gene (9), variant 4	354	355	246..1049

**TABLE 3**

Marker	Gene Name	SEQ ID NO (nts)	SEQ ID NO (AAs)	CDS
M604	CLDN10: claudin 10	48	49	36..772
OV14	EVI-1: Evi-1 protein, variant 2	78	79	250..3405
OV15	EVI-1: Evi-1 protein, variant 3	80	81	250..2433
OV16	EVI-1: Evi-1 protein, variant 4	82	83	250..3378
M576	FLJ13710: hypothetical protein FLJ13710	88	89	96..1712
M444	FLJ22316: hypothetical protein FLJ22316	104	105	508..1206
OV30	ITGB8: integrin, beta 8	156	157	681..2990
OV43	MSLN: mesothelin, variant 8	206	205	88..1956

M581	PAEP: progestagen-associated endometrial protein, variant 4	236	233	36..578
M582	PAEP: progestagen-associated endometrial protein, variant 6	239	240	45..521
M466	PAX8: paired box gene 8, isoform 8B, variant 1	244	245	11..1174
M467	PAX8: paired box gene 8, isoform 8C	247	248	161..1357
M468	PAX8: paired box gene 8, isoform 8D	249	250	161..1126
M469	PAX8: paired box gene 8, isoform 8E	251	252	161..1024
OV2	SERPINA1: alpha-1 antitrypsin	285	286	35..1291
M474	Similar to hypothetical protein, MGC: 7199	287	288	173..1053
M590	unnamed gene (10), variant 1	356	357	21..404
M591	unnamed gene (10), variant 2	358	357	21..404
M592	unnamed gene (10), variant 3	359	357	21..404

### Definitions

As used herein, each of the following terms has the meaning associated with it in this section.

The articles "a" and "an" are used herein to refer to one or to more than one (*i.e.* to at least one) of the grammatical object of the article. By way of example, "an element" means one element or more than one element.

A "marker" is a gene whose altered level of expression in a tissue or cell from its expression level in normal or healthy tissue or cell is associated with a disease state, such as cancer. A "marker nucleic acid" is a nucleic acid (*e.g.*, mRNA, cDNA) encoded by or corresponding to a marker of the invention. Such marker nucleic acids can be DNA (*e.g.*, cDNA) comprising the sequences listed in Table 1 or the complement of such sequences. The marker nucleic acids also can be RNA comprising the sequences listed in Table 1 or the complement of such sequence, wherein all thymidine residues are replaced with uridine residues. A "marker protein" is a protein encoded by or corresponding to a marker of the invention. A marker protein comprises the sequence of any of the sequences listed in Table 1. The terms "protein" and "polypeptide" are used interchangeably.

The term "probe" refers to any molecule which is capable of selectively binding to a specifically intended target molecule, for example, a nucleotide transcript or protein encoded by or corresponding to a marker. Probes can be either synthesized by one skilled in the art, or derived from appropriate biological preparations. For purposes of detection of the target molecule, probes may be specifically designed to be

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labeled, as described herein. Examples of molecules that can be utilized as probes include, but are not limited to, RNA, DNA, proteins, antibodies, and organic molecules.

An "ovary-associated" body fluid is a fluid which, when in the body of a patient, contacts or passes through ovarian cells or into which cells or proteins shed from ovarian cells *e.g.* ovarian epithelium, are capable of passing. Exemplary ovary-associated body fluids include blood fluids, lymph, ascites, gynecological fluids, cystic fluid, urine, and fluids collected by peritoneal rinsing.

The "normal" level of expression of a marker is the level of expression of the marker in ovarian cells of a human subject or patient not afflicted with ovarian cancer

An "over-expression" or "significantly higher level of expression" of a marker refers to an expression level in a test sample that is greater than the standard error of the assay employed to assess expression, and is preferably at least twice, and more preferably three, four, five or ten times the expression level of the marker in a control sample (*e.g.*, sample from a healthy subjects not having the marker associated disease) and preferably, the average expression level of the marker in several control samples.

As used herein, the term "promoter/regulatory sequence" means a nucleic acid sequence which is required for expression of a gene product operably linked to the promoter/regulatory sequence. In some instances, this sequence may be the core promoter sequence and in other instances, this sequence may also include an enhancer sequence and other regulatory elements which are required for expression of the gene product. The promoter/regulatory sequence may, for example, be one which expresses the gene product in a tissue-specific manner.

A "constitutive" promoter is a nucleotide sequence which, when operably linked with a polynucleotide which encodes or specifies a gene product, causes the gene product to be produced in a living human cell under most or all physiological conditions of the cell.

An "inducible" promoter is a nucleotide sequence which, when operably linked with a polynucleotide which encodes or specifies a gene product, causes the gene product to be produced in a living human cell substantially only when an inducer which corresponds to the promoter is present in the cell.

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A "tissue-specific" promoter is a nucleotide sequence which, when operably linked with a polynucleotide which encodes or specifies a gene product, causes the gene product to be produced in a living human cell substantially only if the cell is a cell of the tissue type corresponding to the promoter.

5           A "transcribed polynucleotide" or "nucleotide transcript" is a polynucleotide (*e.g.* an mRNA, hnRNA, a cDNA, or an analog of such RNA or cDNA) which is complementary to or homologous with all or a portion of a mature mRNA made by transcription of a marker of the invention and normal post-transcriptional processing (*e.g.* splicing), if any, of the RNA transcript, and reverse transcription of the  
10   RNA transcript.

"Complementary" refers to the broad concept of sequence complementarity between regions of two nucleic acid strands or between two regions of the same nucleic acid strand. It is known that an adenine residue of a first nucleic acid region is capable of forming specific hydrogen bonds ("base pairing") with a residue of  
15   a second nucleic acid region which is antiparallel to the first region if the residue is thymine or uracil. Similarly, it is known that a cytosine residue of a first nucleic acid strand is capable of base pairing with a residue of a second nucleic acid strand which is antiparallel to the first strand if the residue is guanine. A first region of a nucleic acid is complementary to a second region of the same or a different nucleic acid if, when the  
20   two regions are arranged in an antiparallel fashion, at least one nucleotide residue of the first region is capable of base pairing with a residue of the second region. Preferably, the first region comprises a first portion and the second region comprises a second portion, whereby, when the first and second portions are arranged in an antiparallel fashion, at least about 50%, and preferably at least about 75%, at least about 90%, or at  
25   least about 95% of the nucleotide residues of the first portion are capable of base pairing with nucleotide residues in the second portion. More preferably, all nucleotide residues of the first portion are capable of base pairing with nucleotide residues in the second portion.

"Homologous" as used herein, refers to nucleotide sequence similarity  
30   between two regions of the same nucleic acid strand or between regions of two different nucleic acid strands. When a nucleotide residue position in both regions is occupied by the same nucleotide residue, then the regions are homologous at that position. A first

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- region is homologous to a second region if at least one nucleotide residue position of each region is occupied by the same residue. Homology between two regions is expressed in terms of the proportion of nucleotide residue positions of the two regions that are occupied by the same nucleotide residue. By way of example, a region having
- 5 the nucleotide sequence 5'-ATTGCC-3' and a region having the nucleotide sequence 5'-TATGGC-3' share 50% homology. Preferably, the first region comprises a first portion and the second region comprises a second portion, whereby, at least about 50%, and preferably at least about 75%, at least about 90%, or at least about 95% of the nucleotide residue positions of each of the portions are occupied by the same nucleotide residue.
- 10 More preferably, all nucleotide residue positions of each of the portions are occupied by the same nucleotide residue.

- A molecule is "fixed" or "affixed" to a substrate if it is covalently or non-covalently associated with the substrate such the substrate can be rinsed with a fluid (*e.g.* standard saline citrate, pH 7.4) without a substantial fraction of the molecule
- 15 dissociating from the substrate.

As used herein, a "naturally-occurring" nucleic acid molecule refers to an RNA or DNA molecule having a nucleotide sequence that occurs in an organism found in nature.

- A cancer is "inhibited" if at least one symptom of the cancer is alleviated,
- 20 terminated, slowed, or prevented. As used herein, ovarian cancer is also "inhibited" if recurrence or metastasis of the cancer is reduced, slowed, delayed, or prevented.

- A kit is any manufacture (*e.g.* a package or container) comprising at least one reagent, *e.g.* a probe, for specifically detecting the expression of a marker of the invention. The kit may be promoted, distributed, or sold as a unit for performing the
- 25 methods of the present invention.

- "Proteins of the invention" encompass marker proteins and their fragments; variant marker proteins and their fragments; peptides and polypeptides comprising an at least 15 amino acid segment of a marker or variant marker protein; and fusion proteins comprising a marker or variant marker protein, or an at least 15 amino
- 30 acid segment of a marker or variant marker protein.

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Unless otherwise specified herewithin, the terms “antibody” and “antibodies” broadly encompass naturally-occurring forms of antibodies (*e.g.*, IgG, IgA, IgM, IgE) and recombinant antibodies such as single-chain antibodies, chimeric and humanized antibodies and multi-specific antibodies, as well as fragments and derivatives of all of the foregoing, which fragments and derivatives have at least an antigenic binding site. Antibody derivatives may comprise a protein or chemical moiety conjugated to an antibody moiety.

#### Description

The present invention is based, in part, on newly identified markers which are over-expressed in ovarian cancer cells as compared to their expression in normal (*i.e.* non-cancerous) ovarian cells. The enhanced expression of one or more of these markers in ovarian cells is herein correlated with the cancerous state of the tissue. The invention provides compositions, kits, and methods for assessing the cancerous state of ovarian cells (*e.g.* cells obtained from a human, cultured human cells, archived or preserved human cells and *in vivo* cells) as well as treating patients afflicted with ovarian cancer.

The compositions, kits, and methods of the invention have the following uses, among others:

- 1) assessing whether a patient is afflicted with ovarian cancer;
- 2) assessing the stage of ovarian cancer in a human patient;
- 3) assessing the grade of ovarian cancer in a patient;
- 4) assessing the benign or malignant nature of ovarian cancer in a patient;
- 5) assessing the metastatic potential of ovarian cancer in a patient;
- 6) assessing the histological type of neoplasm (*e.g.* serous, mucinous, endometroid, or clear cell neoplasm) associated with ovarian cancer in a patient;
- 7) making antibodies, antibody fragments or antibody derivatives that are useful for treating ovarian cancer and/or assessing whether a patient is afflicted with ovarian cancer;

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- 8) assessing the presence of ovarian cancer cells;
- 9) assessing the efficacy of one or more test compounds for inhibiting ovarian cancer in a patient;
- 10) assessing the efficacy of a therapy for inhibiting ovarian cancer in a patient;
- 11) monitoring the progression of ovarian cancer in a patient;
- 12) selecting a composition or therapy for inhibiting ovarian cancer in a patient;
- 13) treating a patient afflicted with ovarian cancer;
- 14) inhibiting ovarian cancer in a patient;
- 15) assessing the ovarian carcinogenic potential of a test compound; and
- 16) preventing the onset of ovarian cancer in a patient at risk for developing ovarian cancer.

The invention thus includes a method of assessing whether a patient is afflicted with ovarian cancer which includes assessing whether the patient has pre-metastasized ovarian cancer. This method comprises comparing the level of expression of a marker of the invention (listed in Table 1) in a patient sample and the normal level of expression of the marker in a control, *e.g.*, a non-ovarian cancer sample. A significantly higher level of expression of the marker in the patient sample as compared to the normal level is an indication that the patient is afflicted with ovarian cancer.

Gene delivery vehicles, host cells and compositions (all described herein) containing nucleic acids comprising the entirety, or a segment of 15 or more nucleotides, of any of the sequences listed in Tables 1-3 or the complement of such sequences, and polypeptides comprising the entirety, or a segment of 10 or more amino acids, of any of the sequences listed in Tables 1-3 are also provided by this invention.

As described herein, ovarian cancer in patients is associated with an increased level of expression of one or more markers of the invention. While, as discussed above, some of these changes in expression level result from occurrence of the ovarian cancer, others of these changes induce, maintain, and promote the cancerous state of ovarian cancer cells. Thus, ovarian cancer characterized by an increase in the level of expression of one or more markers of the invention can be inhibited by reducing

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and/or interfering with the expression of the markers and/or function of the proteins encoded by those markers.

Expression of a marker of the invention can be inhibited in a number of ways generally known in the art. For example, an antisense oligonucleotide can be provided to the ovarian cancer cells in order to inhibit transcription, translation, or both, of the marker(s). Alternately, a polynucleotide encoding an antibody, an antibody derivative, or an antibody fragment which specifically binds a marker protein, and operably linked with an appropriate promoter/regulator region, can be provided to the cell in order to generate intracellular antibodies which will inhibit the function or activity of the protein. The expression and/or function of a marker may also be inhibited by treating the ovarian cancer cell with an antibody, antibody derivative or antibody fragment that specifically binds a marker protein. Using the methods described herein, a variety of molecules, particularly including molecules sufficiently small that they are able to cross the cell membrane, can be screened in order to identify molecules which inhibit expression of a marker or inhibit the function of a marker protein. The compound so identified can be provided to the patient in order to inhibit ovarian cancer cells of the patient.

Any marker or combination of markers of the invention, as well as any known markers in combination with the markers of the invention, may be used in the compositions, kits, and methods of the present invention. In general, it is preferable to use markers for which the difference between the level of expression of the marker in ovarian cancer cells and the level of expression of the same marker in normal ovarian cells is as great as possible. Although this difference can be as small as the limit of detection of the method for assessing expression of the marker, it is preferred that the difference be at least greater than the standard error of the assessment method, and preferably a difference of at least 2-, 3-, 4-, 5-, 6-, 7-, 8-, 9-, 10-, 15-, 20-, 25-, 100-, 500-, 1000-fold or greater than the level of expression of the same marker in normal ovarian tissue.

It is recognized that certain marker proteins are secreted from ovarian cells (*i.e.* one or both of normal and cancerous cells) to the extracellular space surrounding the cells. These markers are preferably used in certain embodiments of the compositions, kits, and methods of the invention, owing to the fact that the such marker

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proteins can be detected in an ovary-associated body fluid sample, which may be more easily collected from a human patient than a tissue biopsy sample. In addition, preferred *in vivo* techniques for detection of a marker protein include introducing into a subject a labeled antibody directed against the protein. For example, the antibody can be labeled  
5 with a radioactive marker whose presence and location in a subject can be detected by standard imaging techniques.

It is a simple matter for the skilled artisan to determine whether any particular marker protein is a secreted protein. In order to make this determination, the marker protein is expressed in, for example, a mammalian cell, preferably a human  
10 ovarian cell line, extracellular fluid is collected, and the presence or absence of the protein in the extracellular fluid is assessed (e.g. using a labeled antibody which binds specifically with the protein).

The following is an example of a method which can be used to detect secretion of a protein. About  $8 \times 10^5$  293T cells are incubated at 37°C in wells  
15 containing growth medium (Dulbecco's modified Eagle's medium {DMEM} supplemented with 10% fetal bovine serum) under a 5% (v/v) CO<sub>2</sub>, 95% air atmosphere to about 60-70% confluence. The cells are then transfected using a standard transfection mixture comprising 2 micrograms of DNA comprising an expression vector encoding the protein and 10 microliters of LipofectAMINE™ (GIBCO/BRL Catalog no. 18342-  
20 012) per well. The transfection mixture is maintained for about 5 hours, and then replaced with fresh growth medium and maintained in an air atmosphere. Each well is gently rinsed twice with DMEM which does not contain methionine or cysteine (DMEM-MC; ICN Catalog no. 16-424- 54). About 1 milliliter of DMEM-MC and about 50 microcuries of Trans-<sup>35</sup>S™ reagent (ICN Catalog no. 51006) are added to each  
25 well. The wells are maintained under the 5% CO<sub>2</sub> atmosphere described above and incubated at 37°C for a selected period. Following incubation, 150 microliters of conditioned medium is removed and centrifuged to remove floating cells and debris. The presence of the protein in the supernatant is an indication that the protein is secreted.

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Examples of ovary-associated body fluids include blood fluids (*e.g.* whole blood, blood serum, blood having platelets removed therefrom, etc.), lymph, ascitic fluids, gynecological fluids (*e.g.* ovarian, fallopian, and uterine secretions, menses, vaginal douching fluids, fluids used to rinse ovarian cell samples, etc.), cystic  
5 fluid, urine, and fluids collected by peritoneal rinsing (*e.g.* fluids applied and collected during laparoscopy or fluids instilled into and withdrawn from the peritoneal cavity of a human patient). In these embodiments, the level of expression of the marker can be assessed by assessing the amount (*e.g.* absolute amount or concentration) of the marker protein in an ovary-associated body fluid obtained from a patient. The fluid can, of  
10 course, be subjected to a variety of well-known post-collection preparative and storage techniques (*e.g.* storage, freezing, ultrafiltration, concentration, evaporation, centrifugation, etc.) prior to assessing the amount of the marker in the fluid.

Many ovary-associated body fluids (*i.e.* usually excluding urine) can have ovarian cells, *e.g.* ovarian epithelium, therein, particularly when the ovarian cells  
15 are cancerous, and, more particularly, when the ovarian cancer is metastasizing. Cell-containing fluids which can contain ovarian cancer cells include, but are not limited to, peritoneal ascites, fluids collected by peritoneal rinsing, fluids collected by uterine rinsing, uterine fluids such as uterine exudate and menses, pleural fluid, and ovarian exudates. Thus, the compositions, kits, and methods of the invention can be used to  
20 detect expression of marker proteins having at least one portion which is displayed on the surface of cells which express it. It is a simple matter for the skilled artisan to determine whether a marker protein, or a portion thereof, is exposed on the cell surface. For example, immunological methods may be used to detect such proteins on whole cells, or well known computer-based sequence analysis methods (*e.g.* the SIGNALP  
25 program; Nielsen *et al.*, 1997, *Protein Engineering* 10:1-6) may be used to predict the presence of at least one extracellular domain (*i.e.* including both secreted proteins and proteins having at least one cell-surface domain). Expression of a marker protein having at least one portion which is displayed on the surface of a cell which expresses it may be detected without necessarily lysing the cell (*e.g.* using a labeled antibody which binds  
30 specifically with a cell-surface domain of the protein).

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Expression of a marker of the invention may be assessed by any of a wide variety of well known methods for detecting expression of a transcribed nucleic acid or protein. Non-limiting examples of such methods include immunological methods for detection of secreted, cell-surface, cytoplasmic, or nuclear proteins, protein  
5 purification methods, protein function or activity assays, nucleic acid hybridization methods, nucleic acid reverse transcription methods, and nucleic acid amplification methods.

In a preferred embodiment, expression of a marker is assessed using an antibody (*e.g.* a radio-labeled, chromophore-labeled, fluorophore-labeled, or enzyme-  
10 labeled antibody), an antibody derivative (*e.g.* an antibody conjugated with a substrate or with the protein or ligand of a protein-ligand pair {*e.g.* biotin-streptavidin} ), or an antibody fragment (*e.g.* a single-chain antibody, an isolated antibody hypervariable domain, etc.) or derivative which binds specifically with a marker protein or fragment thereof, including a marker protein which has undergone all or a portion of its normal  
15 post-translational modification.

In another preferred embodiment, expression of a marker is assessed by preparing mRNA/cDNA (*i.e.* a transcribed polynucleotide) from cells in a patient sample, and by hybridizing the mRNA/cDNA with a reference polynucleotide which is a complement of a marker nucleic acid, or a fragment thereof. cDNA can, optionally, be  
20 amplified using any of a variety of polymerase chain reaction methods prior to hybridization with the reference polynucleotide; preferably, it is not amplified. Expression of one or more markers can likewise be detected using quantitative PCR to assess the level of expression of the marker(s). Alternatively, any of the many known methods of detecting mutations or variants (*e.g.* single nucleotide polymorphisms,  
25 deletions, etc.) of a marker of the invention may be used to detect occurrence of a marker in a patient.

In a related embodiment, a mixture of transcribed polynucleotides obtained from the sample is contacted with a substrate having fixed thereto a polynucleotide complementary to or homologous with at least a portion (*e.g.* at least 7,  
30 10, 15, 20, 25, 30, 40, 50, 100, 500, or more nucleotide residues) of a marker nucleic acid. If polynucleotides complementary to or homologous with several marker nucleic acids are differentially detectable on the substrate (*e.g.* detectable using different

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chromophores or fluorophores, or fixed to different selected positions), then the levels of expression of a plurality of markers can be assessed simultaneously using a single substrate (e.g. a "gene chip" microarray of polynucleotides fixed at selected positions). When a method of assessing marker expression is used which involves hybridization of one nucleic acid with another, it is preferred that the hybridization be performed under stringent hybridization conditions.

Because the compositions, kits, and methods of the invention rely on detection of a difference in expression levels of one or more markers of the invention, it is preferable that the level of expression of the marker is significantly greater than the minimum detection limit of the method used to assess expression in at least one of normal ovarian cells and cancerous ovarian cells.

It is understood that by routine screening of additional patient samples using one or more of the markers of the invention, it will be realized that certain of the markers are over-expressed in cancers of various types, including specific ovarian cancers, as well as other cancers such as breast cancer, cervical cancer, etc. For example, it will be confirmed that some of the markers of the invention are over-expressed in most (i.e. 50% or more) or substantially all (i.e. 80% or more) of ovarian cancer. Furthermore, it will be confirmed that certain of the markers of the invention are associated with ovarian cancer of various stages (i.e. stage I, II, III, and IV ovarian cancers, as well as subclassifications IA, IB, IC, IIA, IIB, IIC, IIIA, IIIB, and IIIC, using the FIGO Stage Grouping system for primary carcinoma of the ovary; 1987, *Am. J. Obstet. Gynecol.* 156:236), of various histologic subtypes (e.g. serous, mucinous, endometrioid, and clear cell subtypes, as well as subclassifications and alternate classifications adenocarcinoma, papillary adenocarcinoma, papillary cystadenocarcinoma, surface papillary carcinoma, malignant adenofibroma, cystadenofibroma, adenocarcinoma, cystadenocarcinoma, adenoacanthoma, endometrioid stromal sarcoma, mesodermal (Müllerian) mixed tumor, mesonephroid tumor, malignant carcinoma, Brenner tumor, mixed epithelial tumor, and undifferentiated carcinoma, using the WHO/FIGO system for classification of malignant ovarian tumors; Scully, *Atlas of Tumor Pathology*, 3d series, Washington DC), and various grades (i.e. grade I {well differentiated} , grade II {moderately well differentiated}, and grade III {poorly differentiated from surrounding normal tissue} ).

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In addition, as a greater number of patient samples are assessed for expression of the markers of the invention and the outcomes of the individual patients from whom the samples were obtained are correlated, it will also be confirmed that increased expression of certain of the markers of the invention are strongly correlated with malignant cancers and that increased expression of other markers of the invention are strongly correlated with benign tumors. The compositions, kits, and methods of the invention are thus useful for characterizing one or more of the stage, grade, histological type, and benign/malignant nature of ovarian cancer in patients. In addition, these compositions, kits, and methods can be used to detect and differentiate epithelial, stromal, and germ cell ovarian cancers.

When the compositions, kits, and methods of the invention are used for characterizing one or more of the stage, grade, histological type, and benign/malignant nature of ovarian cancer in a patient, it is preferred that the marker or panel of markers of the invention is selected such that a positive result is obtained in at least about 20%, and preferably at least about 40%, 60%, or 80%, and more preferably in substantially all patients afflicted with an ovarian cancer of the corresponding stage, grade, histological type, or benign/malignant nature. Preferably, the marker or panel of markers of the invention is selected such that a PPV of greater than about 10% is obtained for the general population (more preferably coupled with an assay specificity greater than 99.5%).

When a plurality of markers of the invention are used in the compositions, kits, and methods of the invention, the level of expression of each marker in a patient sample can be compared with the normal level of expression of each of the plurality of markers in non-cancerous samples of the same type, either in a single reaction mixture (*i.e.* using reagents, such as different fluorescent probes, for each marker) or in individual reaction mixtures corresponding to one or more of the markers. In one embodiment, a significantly increased level of expression of more than one of the plurality of markers in the sample, relative to the corresponding normal levels, is an indication that the patient is afflicted with ovarian cancer. When a plurality of markers is used, it is preferred that 2, 3, 4, 5, 8, 10, 12, 15, 20, 30, or 50 or more individual markers be used, wherein fewer markers are preferred.

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In order to maximize the sensitivity of the compositions, kits, and methods of the invention (*i.e.* by interference attributable to cells of non-ovarian origin in a patient sample), it is preferable that the marker of the invention used therein be a marker which has a restricted tissue distribution, *e.g.*, normally not expressed in a non-epithelial tissue, and more preferably a marker which is normally not expressed in a non-ovarian tissue.

Only a small number of markers are known to be associated with ovarian cancers (*e.g.* *AKT2*, *Ki-RAS*, *ERBB2*, *c-MYC*, *RB1*, and *TP53*; Lynch, *supra*). These markers are not, of course, included among the markers of the invention, although they may be used together with one or more markers of the invention in a panel of markers, for example. It is well known that certain types of genes, such as oncogenes, tumor suppressor genes, growth factor-like genes, protease-like genes, and protein kinase-like genes are often involved with development of cancers of various types. Thus, among the markers of the invention, use of those which correspond to proteins which resemble proteins encoded by known oncogenes and tumor suppressor genes, and those which correspond to proteins which resemble growth factors, proteases, and protein kinases are preferred.

It is recognized that the compositions, kits, and methods of the invention will be of particular utility to patients having an enhanced risk of developing ovarian cancer and their medical advisors. Patients recognized as having an enhanced risk of developing ovarian cancer include, for example, patients having a familial history of ovarian cancer, patients identified as having a mutant oncogene (*i.e.* at least one allele), and patients of advancing age (*i.e.* women older than about 50 or 60 years).

The level of expression of a marker in normal (*i.e.* non-cancerous) human ovarian tissue can be assessed in a variety of ways. In one embodiment, this normal level of expression is assessed by assessing the level of expression of the marker in a portion of ovarian cells which appears to be non-cancerous and by comparing this normal level of expression with the level of expression in a portion of the ovarian cells which is suspected of being cancerous. For example, when laparoscopy or other medical procedure, reveals the presence of a lump on one portion of a patient's ovary, but not on another portion of the same ovary or on the other ovary, the normal level of expression of a marker may be assessed using one or both of the non-affected ovary and

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a non-affected portion of the affected ovary, and this normal level of expression may be compared with the level of expression of the same marker in an affected portion (*i.e.* the lump) of the affected ovary. Alternately, and particularly as further information becomes available as a result of routine performance of the methods described herein, 5 population-average values for normal expression of the markers of the invention may be used. In other embodiments, the 'normal' level of expression of a marker may be determined by assessing expression of the marker in a patient sample obtained from a non-cancer-afflicted patient, from a patient sample obtained from a patient before the suspected onset of ovarian cancer in the patient, from archived patient samples, and the 10 like.

The invention includes compositions, kits, and methods for assessing the presence of ovarian cancer cells in a sample (*e.g.* an archived tissue sample or a sample obtained from a patient). These compositions, kits, and methods are substantially the same as those described above, except that, where necessary, the compositions, kits, and 15 methods are adapted for use with samples other than patient samples. For example, when the sample to be used is a paraffinized, archived human tissue sample, it can be necessary to adjust the ratio of compounds in the compositions of the invention, in the kits of the invention, or the methods used to assess levels of marker expression in the sample. Such methods are well known in the art and within the skill of the ordinary 20 artisan.

The invention includes a kit for assessing the presence of ovarian cancer cells (*e.g.* in a sample such as a patient sample). The kit comprises a plurality of reagents, each of which is capable of binding specifically with a marker nucleic acid or protein. Suitable reagents for binding with a marker protein include antibodies, 25 antibody derivatives, antibody fragments, and the like. Suitable reagents for binding with a marker nucleic acid (*e.g.* a genomic DNA, an mRNA, a spliced mRNA, a cDNA, or the like) include complementary nucleic acids. For example, the nucleic acid reagents may include oligonucleotides (labeled or non-labeled) fixed to a substrate, labeled oligonucleotides not bound with a substrate, pairs of PCR primers, molecular 30 beacon probes, and the like.

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The kit of the invention may optionally comprise additional components useful for performing the methods of the invention. By way of example, the kit may comprise fluids (*e.g.* SSC buffer) suitable for annealing complementary nucleic acids or for binding an antibody with a protein with which it specifically binds, one or more  
5 sample compartments, an instructional material which describes performance of a method of the invention, a sample of normal ovarian cells, a sample of ovarian cancer cells, and the like.

The invention also includes a method of making an isolated hybridoma which produces an antibody useful for assessing whether patient is afflicted with an  
10 ovarian cancer. In this method, a protein or peptide comprising the entirety or a segment of a marker protein is synthesized or isolated (*e.g.* by purification from a cell in which it is expressed or by transcription and translation of a nucleic acid encoding the protein or peptide *in vivo* or *in vitro* using known methods). A vertebrate, preferably a mammal such as a mouse, rat, rabbit, or sheep, is immunized using the protein or peptide. The  
15 vertebrate may optionally (and preferably) be immunized at least one additional time with the protein or peptide, so that the vertebrate exhibits a robust immune response to the protein or peptide. Splenocytes are isolated from the immunized vertebrate and fused with an immortalized cell line to form hybridomas, using any of a variety of methods well known in the art. Hybridomas formed in this manner are then screened  
20 using standard methods to identify one or more hybridomas which produce an antibody which specifically binds with the marker protein or a fragment thereof. The invention also includes hybridomas made by this method and antibodies made using such hybridomas.

The invention also includes a method of assessing the efficacy of a test  
25 compound for inhibiting ovarian cancer cells. As described above, differences in the level of expression of the markers of the invention correlate with the cancerous state of ovarian cells. Although it is recognized that changes in the levels of expression of certain of the markers of the invention likely result from the cancerous state of ovarian cells, it is likewise recognized that changes in the levels of expression of other of the  
30 markers of the invention induce, maintain, and promote the cancerous state of those cells. Thus, compounds which inhibit an ovarian cancer in a patient will cause the level of expression of one or more of the markers of the invention to change to a level nearer

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the normal level of expression for that marker (*i.e.* the level of expression for the marker in non-cancerous ovarian cells).

This method thus comprises comparing expression of a marker in a first ovarian cell sample and maintained in the presence of the test compound and expression  
5 of the marker in a second ovarian cell sample and maintained in the absence of the test compound. A significantly reduced expression of a marker of the invention in the presence of the test compound is an indication that the test compound inhibits ovarian cancer. The ovarian cell samples may, for example, be aliquots of a single sample of normal ovarian cells obtained from a patient, pooled samples of normal ovarian cells  
10 obtained from a patient, cells of a normal ovarian cell line, aliquots of a single sample of ovarian cancer cells obtained from a patient, pooled samples of ovarian cancer cells obtained from a patient, cells of an ovarian cancer cell line, or the like. In one embodiment, the samples are ovarian cancer cells obtained from a patient and a plurality of compounds known to be effective for inhibiting various ovarian cancers are tested in  
15 order to identify the compound which is likely to best inhibit the ovarian cancer in the patient.

This method may likewise be used to assess the efficacy of a therapy for inhibiting ovarian cancer in a patient. In this method, the level of expression of one or more markers of the invention in a pair of samples (one subjected to the therapy, the  
20 other not subjected to the therapy) is assessed. As with the method of assessing the efficacy of test compounds, if the therapy induces a significantly lower level of expression of a marker of the invention then the therapy is efficacious for inhibiting ovarian cancer. As above, if samples from a selected patient are used in this method, then alternative therapies can be assessed *in vitro* in order to select a therapy most likely  
25 to be efficacious for inhibiting ovarian cancer in the patient.

As described above, the cancerous state of human ovarian cells is correlated with changes in the levels of expression of the markers of the invention. The invention includes a method for assessing the human ovarian cell carcinogenic potential of a test compound. This method comprises maintaining separate aliquots of human  
30 ovarian cells in the presence and absence of the test compound. Expression of a marker of the invention in each of the aliquots is compared. A significantly higher level of expression of a marker of the invention in the aliquot maintained in the presence of the

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test compound (relative to the aliquot maintained in the absence of the test compound) is an indication that the test compound possesses human ovarian cell carcinogenic potential. The relative carcinogenic potentials of various test compounds can be assessed by comparing the degree of enhancement or inhibition of the level of expression of the relevant markers, by comparing the number of markers for which the level of expression is enhanced or inhibited, or by comparing both.

Various aspects of the invention are described in further detail in the following subsections.

#### 10 I. Isolated Nucleic Acid Molecules

One aspect of the invention pertains to isolated nucleic acid molecules, including nucleic acids which encode a marker protein or a portion thereof. Isolated nucleic acids of the invention also include nucleic acid molecules sufficient for use as hybridization probes to identify marker nucleic acid molecules, and fragments of marker nucleic acid molecules, *e.g.*, those suitable for use as PCR primers for the amplification or mutation of marker nucleic acid molecules. As used herein, the term "nucleic acid molecule" is intended to include DNA molecules (*e.g.*, cDNA or genomic DNA) and RNA molecules (*e.g.*, mRNA) and analogs of the DNA or RNA generated using nucleotide analogs. The nucleic acid molecule can be single-stranded or double-stranded, but preferably is double-stranded DNA.

An "isolated" nucleic acid molecule is one which is separated from other nucleic acid molecules which are present in the natural source of the nucleic acid molecule. Preferably, an "isolated" nucleic acid molecule is free of sequences (preferably protein-encoding sequences) which naturally flank the nucleic acid (*i.e.*, sequences located at the 5' and 3' ends of the nucleic acid) in the genomic DNA of the organism from which the nucleic acid is derived. For example, in various embodiments, the isolated nucleic acid molecule can contain less than about 5 kB, 4 kB, 3 kB, 2 kB, 1 kB, 0.5 kB or 0.1 kB of nucleotide sequences which naturally flank the nucleic acid molecule in genomic DNA of the cell from which the nucleic acid is derived. Moreover, an "isolated" nucleic acid molecule, such as a cDNA molecule, can be substantially free of other cellular material, or culture medium when produced by recombinant techniques,

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or substantially free of chemical precursors or other chemicals when chemically synthesized.

A nucleic acid molecule of the present invention can be isolated using standard molecular biology techniques and the sequence information in the database records described herein. Using all or a portion of such nucleic acid sequences, nucleic acid molecules of the invention can be isolated using standard hybridization and cloning techniques (*e.g.*, as described in Sambrook *et al.*, ed., *Molecular Cloning: A Laboratory Manual*, 2nd ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 1989).

A nucleic acid molecule of the invention can be amplified using cDNA, mRNA, or genomic DNA as a template and appropriate oligonucleotide primers according to standard PCR amplification techniques. The nucleic acid so amplified can be cloned into an appropriate vector and characterized by DNA sequence analysis. Furthermore, nucleotides corresponding to all or a portion of a nucleic acid molecule of the invention can be prepared by standard synthetic techniques, *e.g.*, using an automated DNA synthesizer.

In another preferred embodiment, an isolated nucleic acid molecule of the invention comprises a nucleic acid molecule which has a nucleotide sequence complementary to the nucleotide sequence of a marker nucleic acid or to the nucleotide sequence of a nucleic acid encoding a marker protein. A nucleic acid molecule which is complementary to a given nucleotide sequence is one which is sufficiently complementary to the given nucleotide sequence that it can hybridize to the given nucleotide sequence thereby forming a stable duplex.

Moreover, a nucleic acid molecule of the invention can comprise only a portion of a nucleic acid sequence, wherein the full length nucleic acid sequence comprises a marker nucleic acid or which encodes a marker protein. Such nucleic acids can be used, for example, as a probe or primer. The probe/primer typically is used as one or more substantially purified oligonucleotides. The oligonucleotide typically comprises a region of nucleotide sequence that hybridizes under stringent conditions to at least about 7, preferably about 15, more preferably about 25, 50, 75, 100, 125, 150, 175, 200, 250, 300, 350, or 400 or more consecutive nucleotides of a nucleic acid of the invention.

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Probes based on the sequence of a nucleic acid molecule of the invention can be used to detect transcripts or genomic sequences corresponding to one or more markers of the invention. The probe comprises a label group attached thereto, *e.g.*, a radioisotope, a fluorescent compound, an enzyme, or an enzyme co-factor. Such probes  
5 can be used as part of a diagnostic test kit for identifying cells or tissues which mis-express the protein, such as by measuring levels of a nucleic acid molecule encoding the protein in a sample of cells from a subject, *e.g.*, detecting mRNA levels or determining whether a gene encoding the protein has been mutated or deleted.

The invention further encompasses nucleic acid molecules that differ, due  
10 to degeneracy of the genetic code, from the nucleotide sequence of nucleic acids encoding a marker protein and thus encode the same protein.

It will be appreciated by those skilled in the art that DNA sequence polymorphisms that lead to changes in the amino acid sequence can exist within a population (*e.g.*, the human population). Such genetic polymorphisms can exist among  
15 individuals within a population due to natural allelic variation. An allele is one of a group of genes which occur alternatively at a given genetic locus. In addition, it will be appreciated that DNA polymorphisms that affect RNA expression levels can also exist that may affect the overall expression level of that gene (*e.g.*, by affecting regulation or degradation).

20 As used herein, the phrase "allelic variant" refers to a nucleotide sequence which occurs at a given locus or to a polypeptide encoded by the nucleotide sequence.

As used herein, the terms "gene" and "recombinant gene" refer to nucleic acid molecules comprising an open reading frame encoding a polypeptide corresponding  
25 to a marker of the invention. Such natural allelic variations can typically result in 1-5% variance in the nucleotide sequence of a given gene. Alternative alleles can be identified by sequencing the gene of interest in a number of different individuals. This can be readily carried out by using hybridization probes to identify the same genetic locus in a variety of individuals. Any and all such nucleotide variations and resulting amino acid  
30 polymorphisms or variations that are the result of natural allelic variation and that do not alter the functional activity are intended to be within the scope of the invention.

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In another embodiment, an isolated nucleic acid molecule of the invention is at least 7, 15, 20, 25, 30, 40, 60, 80, 100, 150, 200, 250, 300, 350, 400, 450, 550, 650, 700, 800, 900, 1000, 1200, 1400, 1600, 1800, 2000, 2200, 2400, 2600, 2800, 3000, 3500, 4000, 4500, or more nucleotides in length and hybridizes under stringent  
5 conditions to a marker nucleic acid or to a nucleic acid encoding a marker protein. As used herein, the term "hybridizes under stringent conditions" is intended to describe conditions for hybridization and washing under which nucleotide sequences at least 60% (65%, 70%, preferably 75%) identical to each other typically remain hybridized to each other. Such stringent conditions are known to those skilled in the art and can be found  
10 in sections 6.3.1-6.3.6 of *Current Protocols in Molecular Biology*, John Wiley & Sons, N.Y. (1989). A preferred, non-limiting example of stringent hybridization conditions are hybridization in 6X sodium chloride/sodium citrate (SSC) at about 45°C, followed by one or more washes in 0.2X SSC, 0.1% SDS at 50-65°C.

In addition to naturally-occurring allelic variants of a nucleic acid  
15 molecule of the invention that can exist in the population, the skilled artisan will further appreciate that sequence changes can be introduced by mutation thereby leading to changes in the amino acid sequence of the encoded protein, without altering the biological activity of the protein encoded thereby. For example, one can make nucleotide substitutions leading to amino acid substitutions at "non-essential" amino  
20 acid residues. A "non-essential" amino acid residue is a residue that can be altered from the wild-type sequence without altering the biological activity, whereas an "essential" amino acid residue is required for biological activity. For example, amino acid residues that are not conserved or only semi-conserved among homologs of various species may be non-essential for activity and thus would be likely targets for alteration.  
25 Alternatively, amino acid residues that are conserved among the homologs of various species (*e.g.*, murine and human) may be essential for activity and thus would not be likely targets for alteration.

Accordingly, another aspect of the invention pertains to nucleic acid molecules encoding a variant marker protein that contain changes in amino acid residues  
30 that are not essential for activity. Such variant marker proteins differ in amino acid sequence from the naturally-occurring marker proteins, yet retain biological activity. In one embodiment, such a variant marker protein has an amino acid sequence that is at

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least about 40% identical, 50%, 60%, 70%, 80%, 90%, 95%, or 98% identical to the amino acid sequence of a marker protein.

An isolated nucleic acid molecule encoding a variant marker protein can be created by introducing one or more nucleotide substitutions, additions or deletions  
5 into the nucleotide sequence of marker nucleic acids, such that one or more amino acid residue substitutions, additions, or deletions are introduced into the encoded protein. Mutations can be introduced by standard techniques, such as site-directed mutagenesis and PCR-mediated mutagenesis. Preferably, conservative amino acid substitutions are made at one or more predicted non-essential amino acid residues. A "conservative  
10 amino acid substitution" is one in which the amino acid residue is replaced with an amino acid residue having a similar side chain. Families of amino acid residues having similar side chains have been defined in the art. These families include amino acids with basic side chains (*e.g.*, lysine, arginine, histidine), acidic side chains (*e.g.*, aspartic acid, glutamic acid), uncharged polar side chains (*e.g.*, glycine, asparagine, glutamine,  
15 serine, threonine, tyrosine, cysteine), non-polar side chains (*e.g.*, alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan), beta-branched side chains (*e.g.*, threonine, valine, isoleucine) and aromatic side chains (*e.g.*, tyrosine, phenylalanine, tryptophan, histidine). Alternatively, mutations can be introduced randomly along all or part of the coding sequence, such as by saturation mutagenesis,  
20 and the resultant mutants can be screened for biological activity to identify mutants that retain activity. Following mutagenesis, the encoded protein can be expressed recombinantly and the activity of the protein can be determined.

The present invention encompasses antisense nucleic acid molecules, *i.e.*, molecules which are complementary to a sense nucleic acid of the invention, *e.g.*,  
25 complementary to the coding strand of a double-stranded marker cDNA molecule or complementary to a marker mRNA sequence. Accordingly, an antisense nucleic acid of the invention can hydrogen bond to (*i.e.* anneal with) a sense nucleic acid of the invention. The antisense nucleic acid can be complementary to an entire coding strand, or to only a portion thereof, *e.g.*, all or part of the protein coding region (or open reading  
30 frame). An antisense nucleic acid molecule can also be antisense to all or part of a non-coding region of the coding strand of a nucleotide sequence encoding a marker protein.

The non-coding regions ("5' and 3' untranslated regions") are the 5' and 3' sequences which flank the coding region and are not translated into amino acids.

An antisense oligonucleotide can be, for example, about 5, 10, 15, 20, 25, 30, 35, 40, 45, or 50 or more nucleotides in length. An antisense nucleic acid of the invention can be constructed using chemical synthesis and enzymatic ligation reactions using procedures known in the art. For example, an antisense nucleic acid (*e.g.*, an antisense oligonucleotide) can be chemically synthesized using naturally occurring nucleotides or variously modified nucleotides designed to increase the biological stability of the molecules or to increase the physical stability of the duplex formed between the antisense and sense nucleic acids, *e.g.*, phosphorothioate derivatives and acridine substituted nucleotides can be used. Examples of modified nucleotides which can be used to generate the antisense nucleic acid include 5-fluorouracil, 5-bromouracil, 5-chlorouracil, 5-iodouracil, hypoxanthine, xanthine, 4-acetylcytosine, 5-(carboxyhydroxymethyl) uracil, 5-carboxymethylaminomethyl-2-thiouridine, 5-carboxymethylaminomethyluracil, dihydrouracil, beta-D-galactosylqueosine, inosine, N6-isopentenyladenine, 1-methylguanine, 1-methylinosine, 2,2-dimethylguanine, 2-methyladenine, 2-methylguanine, 3-methylcytosine, 5-methylcytosine, N6-adenine, 7-methylguanine, 5-methylaminomethyluracil, 5-methoxyaminomethyl-2-thiouracil, beta-D-mannosylqueosine, 5'-methoxycarboxymethyluracil, 5-methoxyuracil, 2-methylthio-N6-isopentenyladenine, uracil-5-oxyacetic acid (v), wybutoxosine, pseudouracil, queosine, 2-thiocytosine, 5-methyl-2-thiouracil, 2-thiouracil, 4-thiouracil, 5-methyluracil, uracil-5-oxyacetic acid methylester, uracil-5-oxyacetic acid (v), 5-methyl-2-thiouracil, 3-(3-amino-3-N-2-carboxypropyl) uracil, (acp3)w, and 2,6-diaminopurine. Alternatively, the antisense nucleic acid can be produced biologically using an expression vector into which a nucleic acid has been sub-cloned in an antisense orientation (*i.e.*, RNA transcribed from the inserted nucleic acid will be of an antisense orientation to a target nucleic acid of interest, described further in the following subsection).

The antisense nucleic acid molecules of the invention are typically administered to a subject or generated *in situ* such that they hybridize with or bind to cellular mRNA and/or genomic DNA encoding a marker protein to thereby inhibit expression of the marker, *e.g.*, by inhibiting transcription and/or translation. The

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hybridization can be by conventional nucleotide complementarity to form a stable duplex, or, for example, in the case of an antisense nucleic acid molecule which binds to DNA duplexes, through specific interactions in the major groove of the double helix. Examples of a route of administration of antisense nucleic acid molecules of the invention includes direct injection at a tissue site or infusion of the antisense nucleic acid into an ovary-associated body fluid. Alternatively, antisense nucleic acid molecules can be modified to target selected cells and then administered systemically. For example, for systemic administration, antisense molecules can be modified such that they specifically bind to receptors or antigens expressed on a selected cell surface, *e.g.*, by linking the antisense nucleic acid molecules to peptides or antibodies which bind to cell surface receptors or antigens. The antisense nucleic acid molecules can also be delivered to cells using the vectors described herein. To achieve sufficient intracellular concentrations of the antisense molecules, vector constructs in which the antisense nucleic acid molecule is placed under the control of a strong pol II or pol III promoter are preferred.

An antisense nucleic acid molecule of the invention can be an  $\alpha$ -anomeric nucleic acid molecule. An  $\alpha$ -anomeric nucleic acid molecule forms specific double-stranded hybrids with complementary RNA in which, contrary to the usual  $\alpha$ -units, the strands run parallel to each other (Gaultier *et al.*, 1987, *Nucleic Acids Res.* 15:6625-6641). The antisense nucleic acid molecule can also comprise a 2'-*o*-methylribonucleotide (Inoue *et al.*, 1987, *Nucleic Acids Res.* 15:6131-6148) or a chimeric RNA-DNA analogue (Inoue *et al.*, 1987, *FEBS Lett.* 215:327-330).

The invention also encompasses ribozymes. Ribozymes are catalytic RNA molecules with ribonuclease activity which are capable of cleaving a single-stranded nucleic acid, such as an mRNA, to which they have a complementary region. Thus, ribozymes (*e.g.*, hammerhead ribozymes as described in Haselhoff and Gerlach, 1988, *Nature* 334:585-591) can be used to catalytically cleave mRNA transcripts to thereby inhibit translation of the protein encoded by the mRNA. A ribozyme having specificity for a nucleic acid molecule encoding a marker protein can be designed based upon the nucleotide sequence of a cDNA corresponding to the marker. For example, a derivative of a *Tetrahymena* L-19 IVS RNA can be constructed in which the nucleotide sequence of the active site is complementary to the nucleotide sequence to be cleaved

(see Cech *et al.* U.S. Patent No. 4,987,071; and Cech *et al.* U.S. Patent No. 5,116,742). Alternatively, an mRNA encoding a polypeptide of the invention can be used to select a catalytic RNA having a specific ribonuclease activity from a pool of RNA molecules (see, *e.g.*, Bartel and Szostak, 1993, *Science* 261:1411-1418).

5                   The invention also encompasses nucleic acid molecules which form triple helical structures. For example, expression of a marker of the invention can be inhibited by targeting nucleotide sequences complementary to the regulatory region of the gene encoding the marker nucleic acid or protein (*e.g.*, the promoter and/or enhancer) to form triple helical structures that prevent transcription of the gene in target cells. See  
10   generally Helene (1991) *Anticancer Drug Des.* 6(6):569-84; Helene (1992) *Ann. N.Y. Acad. Sci.* 660:27-36; and Maher (1992) *Bioassays* 14(12):807-15.

                  In various embodiments, the nucleic acid molecules of the invention can be modified at the base moiety, sugar moiety or phosphate backbone to improve, *e.g.*, the stability, hybridization, or solubility of the molecule. For example, the deoxyribose  
15   phosphate backbone of the nucleic acids can be modified to generate peptide nucleic acids (see Hyrup *et al.*, 1996, *Bioorganic & Medicinal Chemistry* 4(1): 5-23). As used herein, the terms "peptide nucleic acids" or "PNAs" refer to nucleic acid mimics, *e.g.*, DNA mimics, in which the deoxyribose phosphate backbone is replaced by a pseudopeptide backbone and only the four natural nucleobases are retained. The neutral  
20   backbone of PNAs has been shown to allow for specific hybridization to DNA and RNA under conditions of low ionic strength. The synthesis of PNA oligomers can be performed using standard solid phase peptide synthesis protocols as described in Hyrup *et al.* (1996), *supra*; Perry-O'Keefe *et al.* (1996) *Proc. Natl. Acad. Sci. USA* 93:14670-675.

25                   PNAs can be used in therapeutic and diagnostic applications. For example, PNAs can be used as antisense or antigene agents for sequence-specific modulation of gene expression by, *e.g.*, inducing transcription or translation arrest or inhibiting replication. PNAs can also be used, *e.g.*, in the analysis of single base pair mutations in a gene by, *e.g.*, PNA directed PCR clamping; as artificial restriction  
30   enzymes when used in combination with other enzymes, *e.g.*, S1 nucleases (Hyrup (1996), *supra*; or as probes or primers for DNA sequence and hybridization (Hyrup, 1996, *supra*; Perry-O'Keefe *et al.*, 1996, *Proc. Natl. Acad. Sci. USA* 93:14670-675).

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In another embodiment, PNAs can be modified, *e.g.*, to enhance their stability or cellular uptake, by attaching lipophilic or other helper groups to PNA, by the formation of PNA-DNA chimeras, or by the use of liposomes or other techniques of drug delivery known in the art. For example, PNA-DNA chimeras can be generated

5 which can combine the advantageous properties of PNA and DNA. Such chimeras allow DNA recognition enzymes, *e.g.*, RNase H and DNA polymerases, to interact with the DNA portion while the PNA portion would provide high binding affinity and specificity. PNA-DNA chimeras can be linked using linkers of appropriate lengths selected in terms of base stacking, number of bonds between the nucleobases, and

10 orientation (Hyrup, 1996, *supra*). The synthesis of PNA-DNA chimeras can be performed as described in Hyrup (1996), *supra*, and Finn *et al.* (1996) *Nucleic Acids Res.* 24(17):3357-63. For example, a DNA chain can be synthesized on a solid support using standard phosphoramidite coupling chemistry and modified nucleoside analogs. Compounds such as 5'-(4-methoxytrityl)amino-5'-deoxy-thymidine phosphoramidite can

15 be used as a link between the PNA and the 5' end of DNA (Mag *et al.*, 1989, *Nucleic Acids Res.* 17:5973-88). PNA monomers are then coupled in a step-wise manner to produce a chimeric molecule with a 5' PNA segment and a 3' DNA segment (Finn *et al.*, 1996, *Nucleic Acids Res.* 24(17):3357-63). Alternatively, chimeric molecules can be synthesized with a 5' DNA segment and a 3' PNA segment (Peterser *et al.*, 1975,

20 *Bioorganic Med. Chem. Lett.* 5:1119-11124).

In other embodiments, the oligonucleotide can include other appended groups such as peptides (*e.g.*, for targeting host cell receptors *in vivo*), or agents facilitating transport across the cell membrane (see, *e.g.*, Letsinger *et al.*, 1989, *Proc. Natl. Acad. Sci. USA* 86:6553-6556; Lemaitre *et al.*, 1987, *Proc. Natl. Acad. Sci. USA*

25 84:648-652; PCT Publication No. WO 88/09810) or the blood-brain barrier (see, *e.g.*, PCT Publication No. WO 89/10134). In addition, oligonucleotides can be modified with hybridization-triggered cleavage agents (see, *e.g.*, Krol *et al.*, 1988, *Bio/Techniques* 6:958-976) or intercalating agents (see, *e.g.*, Zon, 1988, *Pharm. Res.* 5:539-549). To this end, the oligonucleotide can be conjugated to another molecule, *e.g.*, a peptide,

30 hybridization triggered cross-linking agent, transport agent, hybridization-triggered cleavage agent, etc.

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The invention also includes molecular beacon nucleic acids having at least one region which is complementary to a nucleic acid of the invention, such that the molecular beacon is useful for quantitating the presence of the nucleic acid of the invention in a sample. A "molecular beacon" nucleic acid is a nucleic acid comprising a pair of complementary regions and having a fluorophore and a fluorescent quencher associated therewith. The fluorophore and quencher are associated with different portions of the nucleic acid in such an orientation that when the complementary regions are annealed with one another, fluorescence of the fluorophore is quenched by the quencher. When the complementary regions of the nucleic acid are not annealed with one another, fluorescence of the fluorophore is quenched to a lesser degree. Molecular beacon nucleic acids are described, for example, in U.S. Patent 5,876,930.

## II. Isolated Proteins and Antibodies

One aspect of the invention pertains to isolated marker proteins and biologically active portions thereof, as well as polypeptide fragments suitable for use as immunogens to raise antibodies directed against a marker protein or a fragment thereof. In one embodiment, the native marker protein can be isolated from cells or tissue sources by an appropriate purification scheme using standard protein purification techniques. In another embodiment, a protein or peptide comprising the whole or a segment of the marker protein is produced by recombinant DNA techniques. Alternative to recombinant expression, such protein or peptide can be synthesized chemically using standard peptide synthesis techniques.

An "isolated" or "purified" protein or biologically active portion thereof is substantially free of cellular material or other contaminating proteins from the cell or tissue source from which the protein is derived, or substantially free of chemical precursors or other chemicals when chemically synthesized. The language "substantially free of cellular material" includes preparations of protein in which the protein is separated from cellular components of the cells from which it is isolated or recombinantly produced. Thus, protein that is substantially free of cellular material includes preparations of protein having less than about 30%, 20%, 10%, or 5% (by dry weight) of heterologous protein (also referred to herein as a "contaminating protein"). When the protein or biologically active portion thereof is recombinantly produced, it is

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also preferably substantially free of culture medium, *i.e.*, culture medium represents less than about 20%, 10%, or 5% of the volume of the protein preparation. When the protein is produced by chemical synthesis, it is preferably substantially free of chemical precursors or other chemicals, *i.e.*, it is separated from chemical precursors or other chemicals which are involved in the synthesis of the protein. Accordingly such preparations of the protein have less than about 30%, 20%, 10%, 5% (by dry weight) of chemical precursors or compounds other than the polypeptide of interest.

Biologically active portions of a marker protein include polypeptides comprising amino acid sequences sufficiently identical to or derived from the amino acid sequence of the marker protein, which include fewer amino acids than the full length protein, and exhibit at least one activity of the corresponding full-length protein. Typically, biologically active portions comprise a domain or motif with at least one activity of the corresponding full-length protein. A biologically active portion of a marker protein of the invention can be a polypeptide which is, for example, 10, 25, 50, 100 or more amino acids in length. Moreover, other biologically active portions, in which other regions of the marker protein are deleted, can be prepared by recombinant techniques and evaluated for one or more of the functional activities of the native form of the marker protein.

Preferred marker proteins are encoded by nucleotide sequences comprising the sequences listed in Tables 1-3. Other useful proteins are substantially identical (*e.g.*, at least about 40%, preferably 50%, 60%, 70%, 80%, 90%, 95%, or 99%) to one of these sequences and retain the functional activity of the corresponding naturally-occurring marker protein yet differ in amino acid sequence due to natural allelic variation or mutagenesis.

To determine the percent identity of two amino acid sequences or of two nucleic acids, the sequences are aligned for optimal comparison purposes (*e.g.*, gaps can be introduced in the sequence of a first amino acid or nucleic acid sequence for optimal alignment with a second amino or nucleic acid sequence). The amino acid residues or nucleotides at corresponding amino acid positions or nucleotide positions are then compared. When a position in the first sequence is occupied by the same amino acid residue or nucleotide as the corresponding position in the second sequence, then the molecules are identical at that position. The percent identity between the two sequences

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is a function of the number of identical positions shared by the sequences (*i.e.*, % identity = # of identical positions/total # of positions (*e.g.*, overlapping positions)  $\times 100$ ). In one embodiment the two sequences are the same length.

The determination of percent identity between two sequences can be accomplished using a mathematical algorithm. A preferred, non-limiting example of a mathematical algorithm utilized for the comparison of two sequences is the algorithm of Karlin and Altschul (1990) *Proc. Natl. Acad. Sci. USA* 87:2264-2268, modified as in Karlin and Altschul (1993) *Proc. Natl. Acad. Sci. USA* 90:5873-5877. Such an algorithm is incorporated into the BLASTN and BLASTX programs of Altschul, *et al.* (1990) *J. Mol. Biol.* 215:403-410. BLAST nucleotide searches can be performed with the BLASTN program, score = 100, wordlength = 12 to obtain nucleotide sequences homologous to a nucleic acid molecules of the invention. BLAST protein searches can be performed with the BLASTP program, score = 50, wordlength = 3 to obtain amino acid sequences homologous to a protein molecules of the invention. To obtain gapped alignments for comparison purposes, a newer version of the BLAST algorithm called Gapped BLAST can be utilized as described in Altschul *et al.* (1997) *Nucleic Acids Res.* 25:3389-3402, which is able to perform gapped local alignments for the programs BLASTN, BLASTP and BLASTX. Alternatively, PSI-Blast can be used to perform an iterated search which detects distant relationships between molecules. When utilizing BLAST, Gapped BLAST, and PSI-Blast programs, the default parameters of the respective programs (*e.g.*, BLASTX and BLASTN) can be used. Another preferred, non-limiting example of a mathematical algorithm utilized for the comparison of sequences is the algorithm of Myers and Miller, (1988) *CABIOS* 4:11-17. Such an algorithm is incorporated into the ALIGN program (version 2.0) which is part of the GCG sequence alignment software package. When utilizing the ALIGN program for comparing amino acid sequences, a PAM120 weight residue table, a gap length penalty of 12, and a gap penalty of 4 can be used. Yet another useful algorithm for identifying regions of local sequence similarity and alignment is the FASTA algorithm as described in Pearson and Lipman (1988) *Proc. Natl. Acad. Sci. USA* 85:2444-2448. When using the FASTA algorithm for comparing nucleotide or amino acid sequences, a PAM120 weight residue table can, for example, be used with a *k*-tuple value of 2.

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The percent identity between two sequences can be determined using techniques similar to those described above, with or without allowing gaps. In calculating percent identity, only exact matches are counted.

The invention also provides chimeric or fusion proteins comprising a marker protein or a segment thereof. As used herein, a "chimeric protein" or "fusion protein" comprises all or part (preferably a biologically active part) of a marker protein operably linked to a heterologous polypeptide (*i.e.*, a polypeptide other than the marker protein). Within the fusion protein, the term "operably linked" is intended to indicate that the marker protein or segment thereof and the heterologous polypeptide are fused in-frame to each other. The heterologous polypeptide can be fused to the amino-terminus or the carboxyl-terminus of the marker protein or segment.

One useful fusion protein is a GST fusion protein in which a marker protein or segment is fused to the carboxyl terminus of GST sequences. Such fusion proteins can facilitate the purification of a recombinant polypeptide of the invention.

In another embodiment, the fusion protein contains a heterologous signal sequence at its amino terminus. For example, the native signal sequence of a marker protein can be removed and replaced with a signal sequence from another protein. For example, the gp67 secretory sequence of the baculovirus envelope protein can be used as a heterologous signal sequence (Ausubel *et al.*, ed., *Current Protocols in Molecular Biology*, John Wiley & Sons, NY, 1992). Other examples of eukaryotic heterologous signal sequences include the secretory sequences of melittin and human placental alkaline phosphatase (Stratagene; La Jolla, California). In yet another example, useful prokaryotic heterologous signal sequences include the phoA secretory signal (Sambrook *et al.*, *supra*) and the protein A secretory signal (Pharmacia Biotech; Piscataway, New Jersey).

In yet another embodiment, the fusion protein is an immunoglobulin fusion protein in which all or part of a marker protein is fused to sequences derived from a member of the immunoglobulin protein family. The immunoglobulin fusion proteins of the invention can be incorporated into pharmaceutical compositions and administered to a subject to inhibit an interaction between a ligand (soluble or membrane-bound) and a protein on the surface of a cell (receptor), to thereby suppress signal transduction *in vivo*. The immunoglobulin fusion protein can be used to affect the bioavailability of a

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- cognate ligand of a marker protein. Inhibition of ligand/receptor interaction can be useful therapeutically, both for treating proliferative and differentiative disorders and for modulating (*e.g.* promoting or inhibiting) cell survival. Moreover, the immunoglobulin fusion proteins of the invention can be used as immunogens to produce antibodies
- 5 directed against a marker protein in a subject, to purify ligands and in screening assays to identify molecules which inhibit the interaction of the marker protein with ligands.

- Chimeric and fusion proteins of the invention can be produced by standard recombinant DNA techniques. In another embodiment, the fusion gene can be synthesized by conventional techniques including automated DNA synthesizers.
- 10 Alternatively, PCR amplification of gene fragments can be carried out using anchor primers which give rise to complementary overhangs between two consecutive gene fragments which can subsequently be annealed and re-amplified to generate a chimeric gene sequence (see, *e.g.*, Ausubel *et al.*, *supra*). Moreover, many expression vectors are commercially available that already encode a fusion moiety (*e.g.*, a GST polypeptide).
- 15 A nucleic acid encoding a polypeptide of the invention can be cloned into such an expression vector such that the fusion moiety is linked in-frame to the polypeptide of the invention.

- A signal sequence can be used to facilitate secretion and isolation of marker proteins. Signal sequences are typically characterized by a core of hydrophobic
- 20 amino acids which are generally cleaved from the mature protein during secretion in one or more cleavage events. Such signal peptides contain processing sites that allow cleavage of the signal sequence from the mature proteins as they pass through the secretory pathway. Thus, the invention pertains to marker proteins, fusion proteins or segments thereof having a signal sequence, as well as to such proteins from which the
- 25 signal sequence has been proteolytically cleaved (*i.e.*, the cleavage products). In one embodiment, a nucleic acid sequence encoding a signal sequence can be operably linked in an expression vector to a protein of interest, such as a marker protein or a segment thereof. The signal sequence directs secretion of the protein, such as from a eukaryotic host into which the expression vector is transformed, and the signal sequence is
- 30 subsequently or concurrently cleaved. The protein can then be readily purified from the extracellular medium by art recognized methods. Alternatively, the signal sequence can

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be linked to the protein of interest using a sequence which facilitates purification, such as with a GST domain.

The present invention also pertains to variants of the marker proteins. Such variants have an altered amino acid sequence which can function as either agonists  
5 (mimetics) or as antagonists. Variants can be generated by mutagenesis, *e.g.*, discrete point mutation or truncation. An agonist can retain substantially the same, or a subset, of the biological activities of the naturally occurring form of the protein. An antagonist of a protein can inhibit one or more of the activities of the naturally occurring form of the protein by, for example, competitively binding to a downstream or upstream member  
10 of a cellular signaling cascade which includes the protein of interest. Thus, specific biological effects can be elicited by treatment with a variant of limited function. Treatment of a subject with a variant having a subset of the biological activities of the naturally occurring form of the protein can have fewer side effects in a subject relative to treatment with the naturally occurring form of the protein.

15 Variants of a marker protein which function as either agonists (mimetics) or as antagonists can be identified by screening combinatorial libraries of mutants, *e.g.*, truncation mutants, of the protein of the invention for agonist or antagonist activity. In one embodiment, a variegated library of variants is generated by combinatorial mutagenesis at the nucleic acid level and is encoded by a variegated gene library. A  
20 variegated library of variants can be produced by, for example, enzymatically ligating a mixture of synthetic oligonucleotides into gene sequences such that a degenerate set of potential protein sequences is expressible as individual polypeptides, or alternatively, as a set of larger fusion proteins (*e.g.*, for phage display). There are a variety of methods which can be used to produce libraries of potential variants of the marker proteins from  
25 a degenerate oligonucleotide sequence. Methods for synthesizing degenerate oligonucleotides are known in the art (see, *e.g.*, Narang, 1983, *Tetrahedron* 39:3; Itakura *et al.*, 1984, *Annu. Rev. Biochem.* 53:323; Itakura *et al.*, 1984, *Science* 198:1056; Ike *et al.*, 1983 *Nucleic Acid Res.* 11:477).

In addition, libraries of segments of a marker protein can be used to  
30 generate a variegated population of polypeptides for screening and subsequent selection of variant marker proteins or segments thereof. For example, a library of coding sequence fragments can be generated by treating a double stranded PCR fragment of the

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coding sequence of interest with a nuclease under conditions wherein nicking occurs only about once per molecule, denaturing the double stranded DNA, renaturing the DNA to form double stranded DNA which can include sense/antisense pairs from different nicked products, removing single stranded portions from reformed duplexes by  
5 treatment with S1 nuclease, and ligating the resulting fragment library into an expression vector. By this method, an expression library can be derived which encodes amino terminal and internal fragments of various sizes of the protein of interest.

Several techniques are known in the art for screening gene products of combinatorial libraries made by point mutations or truncation, and for screening cDNA  
10 libraries for gene products having a selected property. The most widely used techniques, which are amenable to high through-put analysis, for screening large gene libraries typically include cloning the gene library into replicable expression vectors, transforming appropriate cells with the resulting library of vectors, and expressing the combinatorial genes under conditions in which detection of a desired activity facilitates  
15 isolation of the vector encoding the gene whose product was detected. Recursive ensemble mutagenesis (REM), a technique which enhances the frequency of functional mutants in the libraries, can be used in combination with the screening assays to identify variants of a protein of the invention (Arkin and Yourvan, 1992, *Proc. Natl. Acad. Sci. USA* 89:7811-7815; Delgrave *et al.*, 1993, *Protein Engineering* 6(3):327- 331).

20 Another aspect of the invention pertains to antibodies directed against a protein of the invention. In preferred embodiments, the antibodies specifically bind a marker protein or a fragment thereof. The terms "antibody" and "antibodies" as used interchangeably herein refer to immunoglobulin molecules as well as fragments and derivatives thereof that comprise an immunologically active portion of an  
25 immunoglobulin molecule, (*i.e.*, such a portion contains an antigen binding site which specifically binds an antigen, such as a marker protein, *e.g.*, an epitope of a marker protein). An antibody which specifically binds to a protein of the invention is an antibody which binds the protein, but does not substantially bind other molecules in a sample, *e.g.*, a biological sample, which naturally contains the protein. Examples of an  
30 immunologically active portion of an immunoglobulin molecule include, but are not limited to, single-chain antibodies (scAb), F(ab) and F(ab')<sub>2</sub> fragments.

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An isolated protein of the invention or a fragment thereof can be used as an immunogen to generate antibodies. The full-length protein can be used or, alternatively, the invention provides antigenic peptide fragments for use as immunogens. The antigenic peptide of a protein of the invention comprises at least 8 (preferably 10, 15, 20, or 30 or more) amino acid residues of the amino acid sequence of one of the proteins of the invention, and encompasses at least one epitope of the protein such that an antibody raised against the peptide forms a specific immune complex with the protein. Preferred epitopes encompassed by the antigenic peptide are regions that are located on the surface of the protein, *e.g.*, hydrophilic regions. Hydrophobicity sequence analysis, hydrophilicity sequence analysis, or similar analyses can be used to identify hydrophilic regions. In preferred embodiments, an isolated marker protein or fragment thereof is used as an immunogen.

An immunogen typically is used to prepare antibodies by immunizing a suitable (*i.e.* immunocompetent) subject such as a rabbit, goat, mouse, or other mammal or vertebrate. An appropriate immunogenic preparation can contain, for example, recombinantly-expressed or chemically-synthesized protein or peptide. The preparation can further include an adjuvant, such as Freund's complete or incomplete adjuvant, or a similar immunostimulatory agent. Preferred immunogen compositions are those that contain no other human proteins such as, for example, immunogen compositions made using a non-human host cell for recombinant expression of a protein of the invention. In such a manner, the resulting antibody compositions have reduced or no binding of human proteins other than a protein of the invention.

The invention provides polyclonal and monoclonal antibodies. The term "monoclonal antibody" or "monoclonal antibody composition", as used herein, refers to a population of antibody molecules that contain only one species of an antigen binding site capable of immunoreacting with a particular epitope. Preferred polyclonal and monoclonal antibody compositions are ones that have been selected for antibodies directed against a protein of the invention. Particularly preferred polyclonal and monoclonal antibody preparations are ones that contain only antibodies directed against a marker protein or fragment thereof.

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Polyclonal antibodies can be prepared by immunizing a suitable subject with a protein of the invention as an immunogen. The antibody titer in the immunized subject can be monitored over time by standard techniques, such as with an enzyme linked immunosorbent assay (ELISA) using immobilized polypeptide. At an appropriate time after immunization, *e.g.*, when the specific antibody titers are highest, antibody-producing cells can be obtained from the subject and used to prepare monoclonal antibodies (mAb) by standard techniques, such as the hybridoma technique originally described by Kohler and Milstein (1975) *Nature* 256:495-497, the human B cell hybridoma technique (see Kozbor *et al.*, 1983, *Immunol. Today* 4:72), the EBV-hybridoma technique (see Cole *et al.*, pp. 77-96 In *Monoclonal Antibodies and Cancer Therapy*, Alan R. Liss, Inc., 1985) or trioma techniques. The technology for producing hybridomas is well known (see generally *Current Protocols in Immunology*, Coligan *et al.* ed., John Wiley & Sons, New York, 1994). Hybridoma cells producing a monoclonal antibody of the invention are detected by screening the hybridoma culture supernatants for antibodies that bind the polypeptide of interest, *e.g.*, using a standard ELISA assay.

Alternative to preparing monoclonal antibody-secreting hybridomas, a monoclonal antibody directed against a protein of the invention can be identified and isolated by screening a recombinant combinatorial immunoglobulin library (*e.g.*, an antibody phage display library) with the polypeptide of interest. Kits for generating and screening phage display libraries are commercially available (*e.g.*, the Pharmacia *Recombinant Phage Antibody System*, Catalog No. 27-9400-01; and the Stratagene *SurfZAP Phage Display Kit*, Catalog No. 240612). Additionally, examples of methods and reagents particularly amenable for use in generating and screening antibody display library can be found in, for example, U.S. Patent No. 5,223,409; PCT Publication No. WO 92/18619; PCT Publication No. WO 91/17271; PCT Publication No. WO 92/20791; PCT Publication No. WO 92/15679; PCT Publication No. WO 93/01288; PCT Publication No. WO 92/01047; PCT Publication No. WO 92/09690; PCT Publication No. WO 90/02809; Fuchs *et al.* (1991) *Bio/Technology* 9:1370-1372; Hay *et al.* (1992) *Hum. Antibod. Hybridomas* 3:81-85; Huse *et al.* (1989) *Science* 246:1275-1281; Griffiths *et al.* (1993) *EMBO J.* 12:725-734.

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The invention also provides recombinant antibodies that specifically bind a protein of the invention. In preferred embodiments, the recombinant antibodies specifically binds a marker protein or fragment thereof. Recombinant antibodies include, but are not limited to, chimeric and humanized monoclonal antibodies, comprising both human and non-human portions, single-chain antibodies and multi-specific antibodies. A chimeric antibody is a molecule in which different portions are derived from different animal species, such as those having a variable region derived from a murine mAb and a human immunoglobulin constant region. (See, *e.g.*, Cabilly et al., U.S. Patent No. 4,816,567; and Boss et al., U.S. Patent No. 4,816,397, which are incorporated herein by reference in their entirety.) Single-chain antibodies have an antigen binding site and consist of single polypeptides. They can be produced by techniques known in the art, for example using methods described in Ladner *et. al* U.S. Pat. No. 4,946,778 (which is incorporated herein by reference in its entirety); Bird *et al.*, (1988) *Science* 242:423-426; Whitlow *et al.*, (1991) *Methods in Enzymology* 2:1-9; Whitlow *et al.*, (1991) *Methods in Enzymology* 2:97-105; and Huston *et al.*, (1991) *Methods in Enzymology Molecular Design and Modeling: Concepts and Applications* 203:46-88. Multi-specific antibodies are antibody molecules having at least two antigen-binding sites that specifically bind different antigens. Such molecules can be produced by techniques known in the art, for example using methods described in Segal, U.S. Patent No. 4,676,980 (the disclosure of which is incorporated herein by reference in its entirety); Holliger et al., (1993) *Proc. Natl. Acad. Sci. USA* 90:6444-6448; Whitlow *et al.*, (1994) *Protein Eng.* 7:1017-1026 and U.S. Pat. No. 6,121,424.

Humanized antibodies are antibody molecules from non-human species having one or more complementarity determining regions (CDRs) from the non-human species and a framework region from a human immunoglobulin molecule. (See, *e.g.*, Queen, U.S. Patent No. 5,585,089, which is incorporated herein by reference in its entirety.) Humanized monoclonal antibodies can be produced by recombinant DNA techniques known in the art, for example using methods described in PCT Publication No. WO 87/02671; European Patent Application 184,187; European Patent Application 171,496; European Patent Application 173,494; PCT Publication No. WO 86/01533; U.S. Patent No. 4,816,567; European Patent Application 125,023; Better *et al.* (1988) *Science* 240:1041-1043; Liu *et al.* (1987) *Proc. Natl. Acad. Sci. USA* 84:3439-3443; Liu

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- et al.* (1987) *J. Immunol.* 139:3521- 3526; Sun *et al.* (1987) *Proc. Natl. Acad. Sci. USA* 84:214-218; Nishimura *et al.* (1987) *Cancer Res.* 47:999-1005; Wood *et al.* (1985) *Nature* 314:446-449; and Shaw *et al.* (1988) *J. Natl. Cancer Inst.* 80:1553-1559; Morrison (1985) *Science* 229:1202-1207; Oi *et al.* (1986) *Bio/Techniques* 4:214; U.S. Patent 5,225,539; Jones *et al.* (1986) *Nature* 321:552-525; Verhoeyan *et al.* (1988) *Science* 239:1534; and Beidler *et al.* (1988) *J. Immunol.* 141:4053-4060.

- More particularly, humanized antibodies can be produced, for example, using transgenic mice which are incapable of expressing endogenous immunoglobulin heavy and light chains genes, but which can express human heavy and light chain genes.
- 10 The transgenic mice are immunized in the normal fashion with a selected antigen, *e.g.*, all or a portion of a polypeptide corresponding to a marker of the invention. Monoclonal antibodies directed against the antigen can be obtained using conventional hybridoma technology. The human immunoglobulin transgenes harbored by the transgenic mice rearrange during B cell differentiation, and subsequently undergo class
- 15 switching and somatic mutation. Thus, using such a technique, it is possible to produce therapeutically useful IgG, IgA and IgE antibodies. For an overview of this technology for producing human antibodies, see Lonberg and Huszar (1995) *Int. Rev. Immunol.* 13:65-93). For a detailed discussion of this technology for producing human antibodies and human monoclonal antibodies and protocols for producing such antibodies, see, *e.g.*,
- 20 U.S. Patent 5,625,126; U.S. Patent 5,633,425; U.S. Patent 5,569,825; U.S. Patent 5,661,016; and U.S. Patent 5,545,806. In addition, companies such as Abgenix, Inc. (Freemont, CA), can be engaged to provide human antibodies directed against a selected antigen using technology similar to that described above.

- Completely human antibodies which recognize a selected epitope can be
- 25 generated using a technique referred to as "guided selection." In this approach a selected non-human monoclonal antibody, *e.g.*, a murine antibody, is used to guide the selection of a completely human antibody recognizing the same epitope (Jespers *et al.*, 1994, *Bio/technology* 12:899-903).

- The antibodies of the invention can be isolated after production (*e.g.*,
- 30 from the blood or serum of the subject) or synthesis and further purified by well-known techniques. For example, IgG antibodies can be purified using protein A chromatography. Antibodies specific for a protein of the invention can be selected or

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(*e.g.*, partially purified) or purified by, *e.g.*, affinity chromatography. For example, a recombinantly expressed and purified (or partially purified) protein of the invention is produced as described herein, and covalently or non-covalently coupled to a solid support such as, for example, a chromatography column. The column can then be used  
5 to affinity purify antibodies specific for the proteins of the invention from a sample containing antibodies directed against a large number of different epitopes, thereby generating a substantially purified antibody composition, *i.e.*, one that is substantially free of contaminating antibodies. By a substantially purified antibody composition is meant, in this context, that the antibody sample contains at most only 30% (by dry  
10 weight) of contaminating antibodies directed against epitopes other than those of the desired protein of the invention, and preferably at most 20%, yet more preferably at most 10%, and most preferably at most 5% (by dry weight) of the sample is contaminating antibodies. A purified antibody composition means that at least 99% of the antibodies in the composition are directed against the desired protein of the  
15 invention.

In a preferred embodiment, the substantially purified antibodies of the invention may specifically bind to a signal peptide, a secreted sequence, an extracellular domain, a transmembrane or a cytoplasmic domain or cytoplasmic membrane of a protein of the invention. In a particularly preferred embodiment, the substantially  
20 purified antibodies of the invention specifically bind to a secreted sequence or an extracellular domain of the amino acid sequences of a protein of the invention. In a more preferred embodiment, the substantially purified antibodies of the invention specifically bind to a secreted sequence or an extracellular domain of the amino acid sequences of a marker protein.

25 An antibody directed against a protein of the invention can be used to isolate the protein by standard techniques, such as affinity chromatography or immunoprecipitation. Moreover, such an antibody can be used to detect the marker protein or fragment thereof (*e.g.*, in a cellular lysate or cell supernatant) in order to evaluate the level and pattern of expression of the marker. The antibodies can also be  
30 used diagnostically to monitor protein levels in tissues or body fluids (*e.g.* in an ovary-associated body fluid) as part of a clinical testing procedure, *e.g.*, to, for example, determine the efficacy of a given treatment regimen. Detection can be facilitated by the

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use of an antibody derivative, which comprises an antibody of the invention coupled to a detectable substance. Examples of detectable substances include various enzymes, prosthetic groups, fluorescent materials, luminescent materials, bioluminescent materials, and radioactive materials. Examples of suitable enzymes include horseradish

5 peroxidase, alkaline phosphatase,  $\beta$ -galactosidase, or acetylcholinesterase; examples of suitable prosthetic group complexes include streptavidin/biotin and avidin/biotin; examples of suitable fluorescent materials include umbelliferone, fluorescein, fluorescein isothiocyanate, rhodamine, dichlorotriazinylamine fluorescein, dansyl chloride or phycoerythrin; an example of a luminescent material includes luminol;

10 examples of bioluminescent materials include luciferase, luciferin, and aequorin, and examples of suitable radioactive material include  $^{125}\text{I}$ ,  $^{131}\text{I}$ ,  $^{35}\text{S}$  or  $^3\text{H}$ .

Antibodies of the invention may also be used as therapeutic agents in treating cancers. In a preferred embodiment, completely human antibodies of the invention are used for therapeutic treatment of human cancer patients, particularly those

15 having an ovarian cancer. In another preferred embodiment, antibodies that bind specifically to a marker protein or fragment thereof are used for therapeutic treatment. Further, such therapeutic antibody may be an antibody derivative or immunotoxin comprising an antibody conjugated to a therapeutic moiety such as a cytotoxin, a therapeutic agent or a radioactive metal ion. A cytotoxin or cytotoxic agent includes any

20 agent that is detrimental to cells. Examples include taxol, cytochalasin B, gramicidin D, ethidium bromide, emetine, mitomycin, etoposide, tenoposide, vincristine, vinblastine, colchicin, doxorubicin, daunorubicin, dihydroxy anthracin dione, mitoxantrone, mithramycin, actinomycin D, 1-dehydrotestosterone, glucocorticoids, procaine, tetracaine, lidocaine, propranolol, and puromycin and analogs or homologs thereof.

25 Therapeutic agents include, but are not limited to, antimetabolites (*e.g.*, methotrexate, 6-mercaptopurine, 6-thioguanine, cytarabine, 5-fluorouracil decarbazine), alkylating agents (*e.g.*, mechlorethamine, thioepa chlorambucil, melphalan, carmustine (BSNU) and lomustine (CCNU), cyclophosphamide, busulfan, dibromomannitol, streptozotocin, mitomycin C, and cis-dichlorodiamine platinum (II) (DDP) cisplatin), anthracyclines

30 (*e.g.*, daunorubicin (formerly daunomycin) and doxorubicin), antibiotics (*e.g.*, dactinomycin (formerly actinomycin), bleomycin, mithramycin, and anthramycin (AMC)), and anti-mitotic agents (*e.g.*, vincristine and vinblastine).

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The conjugated antibodies of the invention can be used for modifying a given biological response, for the drug moiety is not to be construed as limited to classical chemical therapeutic agents. For example, the drug moiety may be a protein or polypeptide possessing a desired biological activity. Such proteins may include, for example, a toxin such as ribosome-inhibiting protein (see Better et al., U.S. Patent No. 6,146,631, the disclosure of which is incorporated herein in its entirety), abrin, ricin A, pseudomonas exotoxin, or diphtheria toxin; a protein such as tumor necrosis factor, .alpha.-interferon, .beta.-interferon, nerve growth factor, platelet derived growth factor, tissue plasminogen activator; or, biological response modifiers such as, for example, lymphokines, interleukin-1 ("IL-1"), interleukin-2 ("IL-2"), interleukin-6 ("IL-6"), granulocyte macrophage colony stimulating factor ("GM-CSF"), granulocyte colony stimulating factor ("G-CSF"), or other growth factors.

Techniques for conjugating such therapeutic moiety to antibodies are well known, see, *e.g.*, Arnon et al., "Monoclonal Antibodies For Immunotargeting Of Drugs In Cancer Therapy", in *Monoclonal Antibodies And Cancer Therapy*, Reisfeld et al. (eds.), pp. 243-56 (Alan R. Liss, Inc. 1985); Hellstrom et al., "Antibodies For Drug Delivery", in *Controlled Drug Delivery* (2nd Ed.), Robinson et al. (eds.), pp. 623-53 (Marcel Dekker, Inc. 1987); Thorpe, "Antibody Carriers Of Cytotoxic Agents In Cancer Therapy: A Review", in *Monoclonal Antibodies '84: Biological And Clinical Applications*, Pinchera et al. (eds.), pp. 475-506 (1985); "Analysis, Results, And Future Prospective Of The Therapeutic Use Of Radiolabeled Antibody In Cancer Therapy", in *Monoclonal Antibodies For Cancer Detection And Therapy*, Baldwin et al. (eds.), pp. 303-16 (Academic Press 1985), and Thorpe et al., "The Preparation And Cytotoxic Properties Of Antibody-Toxin Conjugates", *Immunol. Rev.*, 62:119-58 (1982).

Accordingly, in one aspect, the invention provides substantially purified antibodies, antibody fragments and derivatives, all of which specifically bind to a protein of the invention and preferably, a marker protein. In various embodiments, the substantially purified antibodies of the invention, or fragments or derivatives thereof, can be human, non-human, chimeric and/or humanized antibodies. In another aspect, the invention provides non-human antibodies, antibody fragments and derivatives, all of which specifically bind to a protein of the invention and preferably, a marker protein. Such non-human antibodies can be goat, mouse, sheep, horse, chicken, rabbit, or rat

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antibodies. Alternatively, the non-human antibodies of the invention can be chimeric and/or humanized antibodies. In addition, the non-human antibodies of the invention can be polyclonal antibodies or monoclonal antibodies. In still a further aspect, the invention provides monoclonal antibodies, antibody fragments and derivatives, all of which specifically bind to a protein of the invention and preferably, a marker protein. The monoclonal antibodies can be human, humanized, chimeric and/or non-human antibodies.

The invention also provides a kit containing an antibody of the invention conjugated to a detectable substance, and instructions for use. Still another aspect of the invention is a pharmaceutical composition comprising an antibody of the invention and a pharmaceutically acceptable carrier. In preferred embodiments, the pharmaceutical composition contains an antibody of the invention, a therapeutic moiety, and a pharmaceutically acceptable carrier.

### 15 III. Recombinant Expression Vectors and Host Cells

Another aspect of the invention pertains to vectors, preferably expression vectors, containing a nucleic acid encoding a marker protein (or a portion of such a protein). As used herein, the term "vector" refers to a nucleic acid molecule capable of transporting another nucleic acid to which it has been linked. One type of vector is a "plasmid", which refers to a circular double stranded DNA loop into which additional DNA segments can be ligated. Another type of vector is a viral vector, wherein additional DNA segments can be ligated into the viral genome. Certain vectors are capable of autonomous replication in a host cell into which they are introduced (*e.g.*, bacterial vectors having a bacterial origin of replication and episomal mammalian vectors). Other vectors (*e.g.*, non-episomal mammalian vectors) are integrated into the genome of a host cell upon introduction into the host cell, and thereby are replicated along with the host genome. Moreover, certain vectors, namely expression vectors, are capable of directing the expression of genes to which they are operably linked. In general, expression vectors of utility in recombinant DNA techniques are often in the form of plasmids (vectors). However, the invention is intended to include such other forms of expression vectors, such as viral vectors (*e.g.*, replication defective

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retroviruses, adenoviruses and adeno-associated viruses), which serve equivalent functions.

The recombinant expression vectors of the invention comprise a nucleic acid of the invention in a form suitable for expression of the nucleic acid in a host cell.

5 This means that the recombinant expression vectors include one or more regulatory sequences, selected on the basis of the host cells to be used for expression, which is operably linked to the nucleic acid sequence to be expressed. Within a recombinant expression vector, "operably linked" is intended to mean that the nucleotide sequence of interest is linked to the regulatory sequence(s) in a manner which allows for expression  
10 of the nucleotide sequence (*e.g.*, in an *in vitro* transcription/translation system or in a host cell when the vector is introduced into the host cell). The term "regulatory sequence" is intended to include promoters, enhancers and other expression control elements (*e.g.*, polyadenylation signals). Such regulatory sequences are described, for example, in Goeddel, *Methods in Enzymology: Gene Expression Technology* vol.185,  
15 Academic Press, San Diego, CA (1991). Regulatory sequences include those which direct constitutive expression of a nucleotide sequence in many types of host cell and those which direct expression of the nucleotide sequence only in certain host cells (*e.g.*, tissue-specific regulatory sequences). It will be appreciated by those skilled in the art that the design of the expression vector can depend on such factors as the choice of the  
20 host cell to be transformed, the level of expression of protein desired, and the like. The expression vectors of the invention can be introduced into host cells to thereby produce proteins or peptides, including fusion proteins or peptides, encoded by nucleic acids as described herein.

The recombinant expression vectors of the invention can be designed for  
25 expression of a marker protein or a segment thereof in prokaryotic (*e.g.*, *E. coli*) or eukaryotic cells (*e.g.*, insect cells {using baculovirus expression vectors}, yeast cells or mammalian cells). Suitable host cells are discussed further in Goeddel, *supra*. Alternatively, the recombinant expression vector can be transcribed and translated *in vitro*, for example using T7 promoter regulatory sequences and T7 polymerase.

30 Expression of proteins in prokaryotes is most often carried out in *E. coli* with vectors containing constitutive or inducible promoters directing the expression of either fusion or non-fusion proteins. Fusion vectors add a number of amino acids to a

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protein encoded therein, usually to the amino terminus of the recombinant protein. Such fusion vectors typically serve three purposes: 1) to increase expression of recombinant protein; 2) to increase the solubility of the recombinant protein; and 3) to aid in the purification of the recombinant protein by acting as a ligand in affinity purification.

- 5 Often, in fusion expression vectors, a proteolytic cleavage site is introduced at the junction of the fusion moiety and the recombinant protein to enable separation of the recombinant protein from the fusion moiety subsequent to purification of the fusion protein. Such enzymes, and their cognate recognition sequences, include Factor Xa, thrombin and enterokinase. Typical fusion expression vectors include pGEX
- 10 (Pharmacia Biotech Inc; Smith and Johnson, 1988, *Gene* 67:31-40), pMAL (New England Biolabs, Beverly, MA) and pRIT5 (Pharmacia, Piscataway, NJ) which fuse glutathione S-transferase (GST), maltose E binding protein, or protein A, respectively, to the target recombinant protein.

Examples of suitable inducible non-fusion *E. coli* expression vectors

- 15 include pTrc (Amann *et al.*, 1988, *Gene* 69:301-315) and pET 11d (Studier *et al.*, p. 60-89, In *Gene Expression Technology: Methods in Enzymology* vol.185, Academic Press, San Diego, CA, 1991). Target gene expression from the pTrc vector relies on host RNA polymerase transcription from a hybrid trp-lac fusion promoter. Target gene expression from the pET 11d vector relies on transcription from a T7 gn10-lac fusion promoter
- 20 mediated by a co-expressed viral RNA polymerase (T7 gn1). This viral polymerase is supplied by host strains BL21(DE3) or HMS174(DE3) from a resident prophage harboring a T7 gn1 gene under the transcriptional control of the lacUV 5 promoter.

- One strategy to maximize recombinant protein expression in *E. coli* is to express the protein in a host bacteria with an impaired capacity to proteolytically cleave
- 25 the recombinant protein (Gottesman, p. 119-128, In *Gene Expression Technology: Methods in Enzymology* vol. 185, Academic Press, San Diego, CA, 1990. Another strategy is to alter the nucleic acid sequence of the nucleic acid to be inserted into an expression vector so that the individual codons for each amino acid are those preferentially utilized in *E. coli* (Wada *et al.*, 1992, *Nucleic Acids Res.* 20:2111-2118).
- 30 Such alteration of nucleic acid sequences of the invention can be carried out by standard DNA synthesis techniques.

In another embodiment, the expression vector is a yeast expression vector. Examples of vectors for expression in yeast *S. cerevisiae* include pYepSec1 (Baldari *et al.*, 1987, *EMBO J.* 6:229-234), pMFa (Kurjan and Herskowitz, 1982, *Cell* 30:933-943), pJRY88 (Schultz *et al.*, 1987, *Gene* 54:113-123), pYES2 (Invitrogen Corporation, San Diego, CA), and pPicZ (Invitrogen Corp, San Diego, CA).

Alternatively, the expression vector is a baculovirus expression vector. Baculovirus vectors available for expression of proteins in cultured insect cells (*e.g.*, Sf 9 cells) include the pAc series (Smith *et al.*, 1983, *Mol. Cell Biol.* 3:2156-2165) and the pVL series (Lucklow and Summers, 1989, *Virology* 170:31-39).

In yet another embodiment, a nucleic acid of the invention is expressed in mammalian cells using a mammalian expression vector. Examples of mammalian expression vectors include pCDM8 (Seed, 1987, *Nature* 329:840) and pMT2PC (Kaufman *et al.*, 1987, *EMBO J.* 6:187-195). When used in mammalian cells, the expression vector's control functions are often provided by viral regulatory elements. For example, commonly used promoters are derived from polyoma, Adenovirus 2, cytomegalovirus and Simian Virus 40. For other suitable expression systems for both prokaryotic and eukaryotic cells see chapters 16 and 17 of Sambrook *et al.*, *supra*.

In another embodiment, the recombinant mammalian expression vector is capable of directing expression of the nucleic acid preferentially in a particular cell type (*e.g.*, tissue-specific regulatory elements are used to express the nucleic acid). Tissue-specific regulatory elements are known in the art. Non-limiting examples of suitable tissue-specific promoters include the albumin promoter (liver-specific; Pinkert *et al.*, 1987, *Genes Dev.* 1:268-277), lymphoid-specific promoters (Calame and Eaton, 1988, *Adv. Immunol.* 43:235-275), in particular promoters of T cell receptors (Winoto and Baltimore, 1989, *EMBO J.* 8:729-733) and immunoglobulins (Banerji *et al.*, 1983, *Cell* 33:729-740; Queen and Baltimore, 1983, *Cell* 33:741-748), neuron-specific promoters (*e.g.*, the neurofilament promoter; Byrne and Ruddle, 1989, *Proc. Natl. Acad. Sci. USA* 86:5473-5477), pancreas-specific promoters (Edlund *et al.*, 1985, *Science* 230:912-916), and mammary gland-specific promoters (*e.g.*, milk whey promoter; U.S. Patent No. 4,873,316 and European Application Publication No. 264,166). Developmentally-regulated promoters are also encompassed, for example the murine hox promoters

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(Kessel and Gruss, 1990, *Science* 249:374-379) and the  $\alpha$ -fetoprotein promoter (Camper and Tilghman, 1989, *Genes Dev.* 3:537-546).

The invention further provides a recombinant expression vector comprising a DNA molecule of the invention cloned into the expression vector in an antisense orientation. That is, the DNA molecule is operably linked to a regulatory sequence in a manner which allows for expression (by transcription of the DNA molecule) of an RNA molecule which is antisense to the mRNA encoding a polypeptide of the invention. Regulatory sequences operably linked to a nucleic acid cloned in the antisense orientation can be chosen which direct the continuous expression of the antisense RNA molecule in a variety of cell types, for instance viral promoters and/or enhancers, or regulatory sequences can be chosen which direct constitutive, tissue-specific or cell type specific expression of antisense RNA. The antisense expression vector can be in the form of a recombinant plasmid, phagemid, or attenuated virus in which antisense nucleic acids are produced under the control of a high efficiency regulatory region, the activity of which can be determined by the cell type into which the vector is introduced. For a discussion of the regulation of gene expression using antisense genes see Weintraub *et al.*, 1986, *Trends in Genetics*, Vol. 1(1).

Another aspect of the invention pertains to host cells into which a recombinant expression vector of the invention has been introduced. The terms "host cell" and "recombinant host cell" are used interchangeably herein. It is understood that such terms refer not only to the particular subject cell but to the progeny or potential progeny of such a cell. Because certain modifications may occur in succeeding generations due to either mutation or environmental influences, such progeny may not, in fact, be identical to the parent cell, but are still included within the scope of the term as used herein.

A host cell can be any prokaryotic (*e.g.*, *E. coli*) or eukaryotic cell (*e.g.*, insect cells, yeast or mammalian cells).

Vector DNA can be introduced into prokaryotic or eukaryotic cells via conventional transformation or transfection techniques. As used herein, the terms "transformation" and "transfection" are intended to refer to a variety of art-recognized techniques for introducing foreign nucleic acid into a host cell, including calcium phosphate or calcium chloride co-precipitation, DEAE-dextran-mediated transfection,

lipofection, or electroporation. Suitable methods for transforming or transfecting host cells can be found in Sambrook, *et al. (supra)*, and other laboratory manuals.

For stable transfection of mammalian cells, it is known that, depending upon the expression vector and transfection technique used, only a small fraction of cells  
5 may integrate the foreign DNA into their genome. In order to identify and select these integrants, a gene that encodes a selectable marker (*e.g.*, for resistance to antibiotics) is generally introduced into the host cells along with the gene of interest. Preferred selectable markers include those which confer resistance to drugs, such as G418, hygromycin and methotrexate. Cells stably transfected with the introduced nucleic acid  
10 can be identified by drug selection (*e.g.*, cells that have incorporated the selectable marker gene will survive, while the other cells die).

A host cell of the invention, such as a prokaryotic or eukaryotic host cell in culture, can be used to produce a marker protein or a segment thereof. Accordingly, the invention further provides methods for producing a marker protein or a segment  
15 thereof using the host cells of the invention. In one embodiment, the method comprises culturing the host cell of the invention (into which a recombinant expression vector encoding a marker protein or a segment thereof has been introduced) in a suitable medium such that the is produced. In another embodiment, the method further comprises isolating the a marker protein or a segment thereof from the medium or the  
20 host cell.

The host cells of the invention can also be used to produce nonhuman transgenic animals. For example, in one embodiment, a host cell of the invention is a fertilized oocyte or an embryonic stem cell into which a sequences encoding a marker protein or a segment thereof have been introduced. Such host cells can then be used to  
25 create non-human transgenic animals in which exogenous sequences encoding a marker protein of the invention have been introduced into their genome or homologous recombinant animals in which endogenous gene(s) encoding a marker protein have been altered. Such animals are useful for studying the function and/or activity of the marker protein and for identifying and/or evaluating modulators of marker protein. As used  
30 herein, a "transgenic animal" is a non-human animal, preferably a mammal, more preferably a rodent such as a rat or mouse, in which one or more of the cells of the animal includes a transgene. Other examples of transgenic animals include non-human

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primates, sheep, dogs, cows, goats, chickens, amphibians, etc. A transgene is exogenous DNA which is integrated into the genome of a cell from which a transgenic animal develops and which remains in the genome of the mature animal, thereby directing the expression of an encoded gene product in one or more cell types or tissues of the

5 transgenic animal. As used herein, an "homologous recombinant animal" is a non-human animal, preferably a mammal, more preferably a mouse, in which an endogenous gene has been altered by homologous recombination between the endogenous gene and an exogenous DNA molecule introduced into a cell of the animal, *e.g.*, an embryonic cell of the animal, prior to development of the animal.

10 A transgenic animal of the invention can be created by introducing a nucleic acid encoding a marker protein into the male pronuclei of a fertilized oocyte, *e.g.*, by microinjection, retroviral infection, and allowing the oocyte to develop in a pseudopregnant female foster animal. Intronic sequences and polyadenylation signals can also be included in the transgene to increase the efficiency of expression of the

15 transgene. A tissue-specific regulatory sequence(s) can be operably linked to the transgene to direct expression of the polypeptide of the invention to particular cells. Methods for generating transgenic animals via embryo manipulation and microinjection, particularly animals such as mice, have become conventional in the art and are described, for example, in U.S. Patent Nos. 4,736,866 and 4,870,009, U.S. Patent No.

20 4,873,191 and in Hogan, *Manipulating the Mouse Embryo*, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y., 1986. Similar methods are used for production of other transgenic animals. A transgenic founder animal can be identified based upon the presence of the transgene in its genome and/or expression of mRNA encoding the transgene in tissues or cells of the animals. A transgenic founder animal

25 can then be used to breed additional animals carrying the transgene. Moreover, transgenic animals carrying the transgene can further be bred to other transgenic animals carrying other transgenes.

To create an homologous recombinant animal, a vector is prepared which contains at least a portion of a gene encoding a marker protein into which a deletion,

30 addition or substitution has been introduced to thereby alter, *e.g.*, functionally disrupt, the gene. In a preferred embodiment, the vector is designed such that, upon homologous recombination, the endogenous gene is functionally disrupted (*i.e.*, no longer encodes a

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functional protein; also referred to as a "knock out" vector). Alternatively, the vector can be designed such that, upon homologous recombination, the endogenous gene is mutated or otherwise altered but still encodes functional protein (e.g., the upstream regulatory region can be altered to thereby alter the expression of the endogenous protein). In the homologous recombination vector, the altered portion of the gene is flanked at its 5' and 3' ends by additional nucleic acid of the gene to allow for homologous recombination to occur between the exogenous gene carried by the vector and an endogenous gene in an embryonic stem cell. The additional flanking nucleic acid sequences are of sufficient length for successful homologous recombination with the endogenous gene. Typically, several kilobases of flanking DNA (both at the 5' and 3' ends) are included in the vector (see, e.g., Thomas and Capecchi, 1987, *Cell* 51:503 for a description of homologous recombination vectors). The vector is introduced into an embryonic stem cell line (e.g., by electroporation) and cells in which the introduced gene has homologously recombined with the endogenous gene are selected (see, e.g., Li *et al.*, 1992, *Cell* 69:915). The selected cells are then injected into a blastocyst of an animal (e.g., a mouse) to form aggregation chimeras (see, e.g., Bradley, *Teratocarcinomas and Embryonic Stem Cells: A Practical Approach*, Robertson, Ed., IRL, Oxford, 1987, pp. 113-152). A chimeric embryo can then be implanted into a suitable pseudopregnant female foster animal and the embryo brought to term. Progeny harboring the homologously recombined DNA in their germ cells can be used to breed animals in which all cells of the animal contain the homologously recombined DNA by germline transmission of the transgene. Methods for constructing homologous recombination vectors and homologous recombinant animals are described further in Bradley (1991) *Current Opinion in Bio/Technology* 2:823-829 and in PCT Publication NOS. WO 90/11354, WO 91/01140, WO 92/0968, and WO 93/04169.

In another embodiment, transgenic non-human animals can be produced which contain selected systems which allow for regulated expression of the transgene. One example of such a system is the *cre/loxP* recombinase system of bacteriophage P1. For a description of the *cre/loxP* recombinase system, see, e.g., Lakso *et al.* (1992) *Proc. Natl. Acad. Sci. USA* 89:6232-6236. Another example of a recombinase system is the FLP recombinase system of *Saccharomyces cerevisiae* (O'Gorman *et al.*, 1991, *Science* 251:1351-1355). If a *cre/loxP* recombinase system is used to regulate expression of the

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transgene, animals containing transgenes encoding both the *Cre* recombinase and a selected protein are required. Such animals can be provided through the construction of "double" transgenic animals, *e.g.*, by mating two transgenic animals, one containing a transgene encoding a selected protein and the other containing a transgene encoding a recombinase.

Clones of the non-human transgenic animals described herein can also be produced according to the methods described in Wilmut *et al.* (1997) *Nature* 385:810-813 and PCT Publication NOS. WO 97/07668 and WO 97/07669.

#### 10 IV. Pharmaceutical Compositions

The nucleic acid molecules, polypeptides, and antibodies (also referred to herein as "active compounds") of the invention can be incorporated into pharmaceutical compositions suitable for administration. Such compositions typically comprise the nucleic acid molecule, protein, or antibody and a pharmaceutically acceptable carrier.

15 As used herein the language "pharmaceutically acceptable carrier" is intended to include any and all solvents, dispersion media, coatings, antibacterial and antifungal agents, isotonic and absorption delaying agents, and the like, compatible with pharmaceutical administration. The use of such media and agents for pharmaceutically active substances is well known in the art. Except insofar as any conventional media or agent  
20 is incompatible with the active compound, use thereof in the compositions is contemplated. Supplementary active compounds can also be incorporated into the compositions.

The invention includes methods for preparing pharmaceutical compositions for modulating the expression or activity of a marker nucleic acid or  
25 protein. Such methods comprise formulating a pharmaceutically acceptable carrier with an agent which modulates expression or activity of a marker nucleic acid or protein. Such compositions can further include additional active agents. Thus, the invention further includes methods for preparing a pharmaceutical composition by formulating a pharmaceutically acceptable carrier with an agent which modulates expression or  
30 activity of a marker nucleic acid or protein and one or more additional active compounds.

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The invention also provides methods (also referred to herein as "screening assays") for identifying modulators, *i.e.*, candidate or test compounds or agents (*e.g.*, peptides, peptidomimetics, peptoids, small molecules or other drugs) which (a) bind to the marker, or (b) have a modulatory (*e.g.*, stimulatory or inhibitory) effect on the activity of the marker or, more specifically, (c) have a modulatory effect on the interactions of the marker with one or more of its natural substrates (*e.g.*, peptide, protein, hormone, co-factor, or nucleic acid), or (d) have a modulatory effect on the expression of the marker. Such assays typically comprise a reaction between the marker and one or more assay components. The other components may be either the test compound itself, or a combination of test compound and a natural binding partner of the marker.

The test compounds of the present invention may be obtained from any available source, including systematic libraries of natural and/or synthetic compounds. Test compounds may also be obtained by any of the numerous approaches in combinatorial library methods known in the art, including: biological libraries; peptoid libraries (libraries of molecules having the functionalities of peptides, but with a novel, non-peptide backbone which are resistant to enzymatic degradation but which nevertheless remain bioactive; see, *e.g.*, Zuckermann *et al.*, 1994, *J. Med. Chem.* 37:2678-85); spatially addressable parallel solid phase or solution phase libraries; synthetic library methods requiring deconvolution; the 'one-bead one-compound' library method; and synthetic library methods using affinity chromatography selection. The biological library and peptoid library approaches are limited to peptide libraries, while the other four approaches are applicable to peptide, non-peptide oligomer or small molecule libraries of compounds (Lam, 1997, *Anticancer Drug Des.* 12:145).

Examples of methods for the synthesis of molecular libraries can be found in the art, for example in: DeWitt *et al.* (1993) *Proc. Natl. Acad. Sci. U.S.A.* 90:6909; Erb *et al.* (1994) *Proc. Natl. Acad. Sci. USA* 91:11422; Zuckermann *et al.* (1994). *J. Med. Chem.* 37:2678; Cho *et al.* (1993) *Science* 261:1303; Carrell *et al.* (1994) *Angew. Chem. Int. Ed. Engl.* 33:2059; Carrell *et al.* (1994) *Angew. Chem. Int. Ed. Engl.* 33:2061; and in Gallop *et al.* (1994) *J. Med. Chem.* 37:1233.

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Libraries of compounds may be presented in solution (*e.g.*, Houghten, 1992, *Biotechniques* 13:412-421), or on beads (Lam, 1991, *Nature* 354:82-84), chips (Fodor, 1993, *Nature* 364:555-556), bacteria and/or spores, (Ladner, USP 5,223,409), plasmids (Cull *et al*, 1992, *Proc Natl Acad Sci USA* 89:1865-1869) or on phage (Scott and Smith, 1990, *Science* 249:386-390; Devlin, 1990, *Science* 249:404-406; Cwirla *et al*, 1990, *Proc. Natl. Acad. Sci.* 87:6378-6382; Felici, 1991, *J. Mol. Biol.* 222:301-310; Ladner, *supra.*).

In one embodiment, the invention provides assays for screening candidate or test compounds which are substrates of a protein encoded by or  
10 corresponding to a marker or biologically active portion thereof. In another embodiment, the invention provides assays for screening candidate or test compounds which bind to a protein encoded by or corresponding to a marker or biologically active portion thereof. Determining the ability of the test compound to directly bind to a protein can be accomplished, for example, by coupling the compound with a  
15 radioisotope or enzymatic label such that binding of the compound to the marker can be determined by detecting the labeled marker compound in a complex. For example, compounds (*e.g.*, marker substrates) can be labeled with  $^{125}\text{I}$ ,  $^{35}\text{S}$ ,  $^{14}\text{C}$ , or  $^3\text{H}$ , either directly or indirectly, and the radioisotope detected by direct counting of radioemission or by scintillation counting. Alternatively, assay components can be enzymatically  
20 labeled with, for example, horseradish peroxidase, alkaline phosphatase, or luciferase, and the enzymatic label detected by determination of conversion of an appropriate substrate to product.

In another embodiment, the invention provides assays for screening candidate or test compounds which modulate the expression of a marker or the activity  
25 of a protein encoded by or corresponding to a marker, or a biologically active portion thereof. In all likelihood, the protein encoded by or corresponding to the marker can, *in vivo*, interact with one or more molecules, such as but not limited to, peptides, proteins, hormones, cofactors and nucleic acids. For the purposes of this discussion, such cellular and extracellular molecules are referred to herein as "binding partners" or marker  
30 "substrate".

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One necessary embodiment of the invention in order to facilitate such screening is the use of a protein encoded by or corresponding to marker to identify the protein's natural *in vivo* binding partners. There are many ways to accomplish this which are known to one skilled in the art. One example is the use of the marker protein  
5 as "bait protein" in a two-hybrid assay or three-hybrid assay (see, *e.g.*, U.S. Patent No. 5,283,317; Zervos *et al.*, 1993, *Cell* 72:223-232; Madura *et al.*, 1993, *J. Biol. Chem.* 268:12046-12054; Bartel *et al.*, 1993, *Biotechniques* 14:920-924; Iwabuchi *et al.*, 1993 *Oncogene* 8:1693-1696; Brent WO94/10300) in order to identify other proteins which bind to or interact with the marker (binding partners) and, therefore, are possibly  
10 involved in the natural function of the marker. Such marker binding partners are also likely to be involved in the propagation of signals by the marker protein or downstream elements of a marker protein-mediated signaling pathway. Alternatively, such marker protein binding partners may also be found to be inhibitors of the marker protein.

The two-hybrid system is based on the modular nature of most  
15 transcription factors, which consist of separable DNA-binding and activation domains. Briefly, the assay utilizes two different DNA constructs. In one construct, the gene that encodes a marker protein fused to a gene encoding the DNA binding domain of a known transcription factor (*e.g.*, GAL-4). In the other construct, a DNA sequence, from a library of DNA sequences, that encodes an unidentified protein ("prey" or "sample") is  
20 fused to a gene that codes for the activation domain of the known transcription factor. If the "bait" and the "prey" proteins are able to interact, *in vivo*, forming a marker-dependent complex, the DNA-binding and activation domains of the transcription factor are brought into close proximity. This proximity allows transcription of a reporter gene (*e.g.*, LacZ) which is operably linked to a transcriptional regulatory site responsive to  
25 the transcription factor. Expression of the reporter gene can be readily detected and cell colonies containing the functional transcription factor can be isolated and used to obtain the cloned gene which encodes the protein which interacts with the marker protein.

In a further embodiment, assays may be devised through the use of the invention for the purpose of identifying compounds which modulate (*e.g.*, affect either  
30 positively or negatively) interactions between a marker protein and its substrates and/or binding partners. Such compounds can include, but are not limited to, molecules such as antibodies, peptides, hormones, oligonucleotides, nucleic acids, and analogs thereof.

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Such compounds may also be obtained from any available source, including systematic libraries of natural and/or synthetic compounds. The preferred assay components for use in this embodiment is an ovarian cancer marker protein identified herein, the known binding partner and/or substrate of same, and the test compound. Test compounds can be  
5 supplied from any source.

The basic principle of the assay systems used to identify compounds that interfere with the interaction between the marker protein and its binding partner involves preparing a reaction mixture containing the marker protein and its binding partner under conditions and for a time sufficient to allow the two products to interact  
10 and bind, thus forming a complex. In order to test an agent for inhibitory activity, the reaction mixture is prepared in the presence and absence of the test compound. The test compound can be initially included in the reaction mixture, or can be added at a time subsequent to the addition of the marker protein and its binding partner. Control reaction mixtures are incubated without the test compound or with a placebo. The  
15 formation of any complexes between the marker protein and its binding partner is then detected. The formation of a complex in the control reaction, but less or no such formation in the reaction mixture containing the test compound, indicates that the compound interferes with the interaction of the marker protein and its binding partner. Conversely, the formation of more complex in the presence of compound than in the  
20 control reaction indicates that the compound may enhance interaction of the marker protein and its binding partner.

The assay for compounds that interfere with the interaction of the marker protein with its binding partner may be conducted in a heterogeneous or homogeneous format. Heterogeneous assays involve anchoring either the marker protein or its binding  
25 partner onto a solid phase and detecting complexes anchored to the solid phase at the end of the reaction. In homogeneous assays, the entire reaction is carried out in a liquid phase. In either approach, the order of addition of reactants can be varied to obtain different information about the compounds being tested. For example, test compounds that interfere with the interaction between the marker proteins and the binding partners  
30 (e.g., by competition) can be identified by conducting the reaction in the presence of the test substance, *i.e.*, by adding the test substance to the reaction mixture prior to or simultaneously with the marker and its interactive binding partner. Alternatively, test

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compounds that disrupt preformed complexes, *e.g.*, compounds with higher binding constants that displace one of the components from the complex, can be tested by adding the test compound to the reaction mixture after complexes have been formed. The various formats are briefly described below.

5                   In a heterogeneous assay system, either the marker protein or its binding partner is anchored onto a solid surface or matrix, while the other corresponding non-anchored component may be labeled, either directly or indirectly. In practice, microtitre plates are often utilized for this approach. The anchored species can be immobilized by a number of methods, either non-covalent or covalent, that are typically well known to  
10 one who practices the art. Non-covalent attachment can often be accomplished simply by coating the solid surface with a solution of the marker protein or its binding partner and drying. Alternatively, an immobilized antibody specific for the assay component to be anchored can be used for this purpose. Such surfaces can often be prepared in advance and stored.

15                   In related embodiments, a fusion protein can be provided which adds a domain that allows one or both of the assay components to be anchored to a matrix. For example, glutathione-S-transferase/marker fusion proteins or glutathione-S-transferase/binding partner can be adsorbed onto glutathione sepharose beads (Sigma Chemical, St. Louis, MO) or glutathione derivatized microtiter plates, which are then  
20 combined with the test compound or the test compound and either the non-adsorbed marker or its binding partner, and the mixture incubated under conditions conducive to complex formation (*e.g.*, physiological conditions). Following incubation, the beads or microtiter plate wells are washed to remove any unbound assay components, the immobilized complex assessed either directly or indirectly, for example, as described  
25 above. Alternatively, the complexes can be dissociated from the matrix, and the level of marker binding or activity determined using standard techniques.

Other techniques for immobilizing proteins on matrices can also be used in the screening assays of the invention. For example, either a marker protein or a marker protein binding partner can be immobilized utilizing conjugation of biotin and  
30 streptavidin. Biotinylated marker protein or target molecules can be prepared from biotin-NHS (N-hydroxy-succinimide) using techniques known in the art (*e.g.*, biotinylation kit, Pierce Chemicals, Rockford, IL), and immobilized in the wells of

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streptavidin-coated 96 well plates (Pierce Chemical). In certain embodiments, the protein-immobilized surfaces can be prepared in advance and stored.

In order to conduct the assay, the corresponding partner of the immobilized assay component is exposed to the coated surface with or without the test compound. After the reaction is complete, unreacted assay components are removed (e.g., by washing) and any complexes formed will remain immobilized on the solid surface. The detection of complexes anchored on the solid surface can be accomplished in a number of ways. Where the non-immobilized component is pre-labeled, the detection of label immobilized on the surface indicates that complexes were formed.

Where the non-immobilized component is not pre-labeled, an indirect label can be used to detect complexes anchored on the surface; e.g., using a labeled antibody specific for the initially non-immobilized species (the antibody, in turn, can be directly labeled or indirectly labeled with, e.g., a labeled anti-Ig antibody). Depending upon the order of addition of reaction components, test compounds which modulate (inhibit or enhance) complex formation or which disrupt preformed complexes can be detected.

In an alternate embodiment of the invention, a homogeneous assay may be used. This is typically a reaction, analogous to those mentioned above, which is conducted in a liquid phase in the presence or absence of the test compound. The formed complexes are then separated from unreacted components, and the amount of complex formed is determined. As mentioned for heterogeneous assay systems, the order of addition of reactants to the liquid phase can yield information about which test compounds modulate (inhibit or enhance) complex formation and which disrupt preformed complexes.

In such a homogeneous assay, the reaction products may be separated from unreacted assay components by any of a number of standard techniques, including but not limited to: differential centrifugation, chromatography, electrophoresis and immunoprecipitation. In differential centrifugation, complexes of molecules may be separated from uncomplexed molecules through a series of centrifugal steps, due to the different sedimentation equilibria of complexes based on their different sizes and densities (see, for example, Rivas, G., and Minton, A.P., *Trends Biochem Sci* 1993 Aug;18(8):284-7). Standard chromatographic techniques may also be utilized to separate complexed molecules from uncomplexed ones. For example, gel filtration

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chromatography separates molecules based on size, and through the utilization of an appropriate gel filtration resin in a column format, for example, the relatively larger complex may be separated from the relatively smaller uncomplexed components. Similarly, the relatively different charge properties of the complex as compared to the uncomplexed molecules may be exploited to differentially separate the complex from the remaining individual reactants, for example through the use of ion-exchange chromatography resins. Such resins and chromatographic techniques are well known to one skilled in the art (see, *e.g.*, Heegaard, 1998, *J Mol. Recognit.* 11:141-148; Hage and Tweed, 1997, *J. Chromatogr. B. Biomed. Sci. Appl.*, 699:499-525). Gel electrophoresis may also be employed to separate complexed molecules from unbound species (see, *e.g.*, Ausubel *et al* (eds.), as described in : Current Protocols in Molecular Biology, J. Wiley & Sons, New York. 1999). In this technique, protein or nucleic acid complexes are separated based on size or charge, for example. In order to maintain the binding interaction during the electrophoretic process, nondenaturing gels in the absence of reducing agent are typically preferred, but conditions appropriate to the particular interactants will be well known to one skilled in the art. Immunoprecipitation is another common technique utilized for the isolation of a protein-protein complex from solution (see, *e.g.*, Ausubel *et al* (eds.), In: Current Protocols in Molecular Biology, J. Wiley & Sons, New York. 1999). In this technique, all proteins binding to an antibody specific to one of the binding molecules are precipitated from solution by conjugating the antibody to a polymer bead that may be readily collected by centrifugation. The bound assay components are released from the beads (through a specific proteolysis event or other technique well known in the art which will not disturb the protein-protein interaction in the complex), and a second immunoprecipitation step is performed, this time utilizing antibodies specific for the correspondingly different interacting assay component. In this manner, only formed complexes should remain attached to the beads. Variations in complex formation in both the presence and the absence of a test compound can be compared, thus offering information about the ability of the compound to modulate interactions between the marker protein and its binding partner.

Also within the scope of the present invention are methods for direct detection of interactions between the marker protein and its natural binding partner and/or a test compound in a homogeneous or heterogeneous assay system without

further sample manipulation. For example, the technique of fluorescence energy transfer may be utilized (see, *e.g.*, Lakowicz *et al.*, U.S. Patent No. 5,631,169; Stavrianopoulos *et al.*, U.S. Patent No. 4,868,103). Generally, this technique involves the addition of a fluorophore label on a first 'donor' molecule (*e.g.*, marker or test compound) such that  
5 its emitted fluorescent energy will be absorbed by a fluorescent label on a second, 'acceptor' molecule (*e.g.*, marker or test compound), which in turn is able to fluoresce due to the absorbed energy. Alternately, the 'donor' protein molecule may simply utilize the natural fluorescent energy of tryptophan residues. Labels are chosen that emit different wavelengths of light, such that the 'acceptor' molecule label may be  
10 differentiated from that of the 'donor'. Since the efficiency of energy transfer between the labels is related to the distance separating the molecules, spatial relationships between the molecules can be assessed. In a situation in which binding occurs between the molecules, the fluorescent emission of the 'acceptor' molecule label in the assay should be maximal. An FET binding event can be conveniently measured through  
15 standard fluorometric detection means well known in the art (*e.g.*, using a fluorimeter). A test substance which either enhances or hinders participation of one of the species in the preformed complex will result in the generation of a signal variant to that of background. In this way, test substances that modulate interactions between a marker and its binding partner can be identified in controlled assays.

20 In another embodiment, modulators of marker expression are identified in a method wherein a cell is contacted with a candidate compound and the expression of marker mRNA or protein in the cell, is determined. The level of expression of marker mRNA or protein in the presence of the candidate compound is compared to the level of expression of marker mRNA or protein in the absence of the candidate  
25 compound. The candidate compound can then be identified as a modulator of marker expression based on this comparison. For example, when expression of marker mRNA or protein is greater (statistically significantly greater) in the presence of the candidate compound than in its absence, the candidate compound is identified as a stimulator of marker mRNA or protein expression. Conversely, when expression of marker mRNA  
30 or protein is less (statistically significantly less) in the presence of the candidate compound than in its absence, the candidate compound is identified as an inhibitor of marker mRNA or protein expression. The level of marker mRNA or protein expression

in the cells can be determined by methods described herein for detecting marker mRNA or protein.

In another aspect, the invention pertains to a combination of two or more of the assays described herein. For example, a modulating agent can be identified using  
5 a cell-based or a cell free assay, and the ability of the agent to modulate the activity of a marker protein can be further confirmed *in vivo*, *e.g.*, in a whole animal model for cellular transformation and/or tumorigenesis.

This invention further pertains to novel agents identified by the above-described screening assays. Accordingly, it is within the scope of this invention to  
10 further use an agent identified as described herein in an appropriate animal model. For example, an agent identified as described herein (*e.g.*, an marker modulating agent, an antisense marker nucleic acid molecule, an marker-specific antibody, or an marker-binding partner) can be used in an animal model to determine the efficacy, toxicity, or side effects of treatment with such an agent. Alternatively, an agent identified as  
15 described herein can be used in an animal model to determine the mechanism of action of such an agent. Furthermore, this invention pertains to uses of novel agents identified by the above-described screening assays for treatments as described herein.

It is understood that appropriate doses of small molecule agents and protein or polypeptide agents depends upon a number of factors within the knowledge of  
20 the ordinarily skilled physician, veterinarian, or researcher. The dose(s) of these agents will vary, for example, depending upon the identity, size, and condition of the subject or sample being treated, further depending upon the route by which the composition is to be administered, if applicable, and the effect which the practitioner desires the agent to have upon the nucleic acid or polypeptide of the invention. Exemplary doses of a small  
25 molecule include milligram or microgram amounts per kilogram of subject or sample weight (*e.g.* about 1 microgram per kilogram to about 500 milligrams per kilogram, about 100 micrograms per kilogram to about 5 milligrams per kilogram, or about 1 microgram per kilogram to about 50 micrograms per kilogram). Exemplary doses of a protein or polypeptide include gram, milligram or microgram amounts per kilogram of  
30 subject or sample weight (*e.g.* about 1 microgram per kilogram to about 5 grams per kilogram, about 100 micrograms per kilogram to about 500 milligrams per kilogram, or about 1 milligram per kilogram to about 50 milligrams per kilogram). It is furthermore

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understood that appropriate doses of one of these agents depend upon the potency of the agent with respect to the expression or activity to be modulated. Such appropriate doses can be determined using the assays described herein. When one or more of these agents is to be administered to an animal (*e.g.* a human) in order to modulate expression or activity of a polypeptide or nucleic acid of the invention, a physician, veterinarian, or researcher can, for example, prescribe a relatively low dose at first, subsequently increasing the dose until an appropriate response is obtained. In addition, it is understood that the specific dose level for any particular animal subject will depend upon a variety of factors including the activity of the specific agent employed, the age, body weight, general health, gender, and diet of the subject, the time of administration, the route of administration, the rate of excretion, any drug combination, and the degree of expression or activity to be modulated.

A pharmaceutical composition of the invention is formulated to be compatible with its intended route of administration. Examples of routes of administration include parenteral, *e.g.*, intravenous, intradermal, subcutaneous, oral (*e.g.*, inhalation), transdermal (topical), transmucosal, and rectal administration. Solutions or suspensions used for parenteral, intradermal, or subcutaneous application can include the following components: a sterile diluent such as water for injection, saline solution, fixed oils, polyethylene glycols, glycerine, propylene glycol or other synthetic solvents; antibacterial agents such as benzyl alcohol or methyl parabens; antioxidants such as ascorbic acid or sodium bisulfite; chelating agents such as ethylenediamine-tetraacetic acid; buffers such as acetates, citrates or phosphates and agents for the adjustment of tonicity such as sodium chloride or dextrose. pH can be adjusted with acids or bases, such as hydrochloric acid or sodium hydroxide. The parenteral preparation can be enclosed in ampules, disposable syringes or multiple dose vials made of glass or plastic.

Pharmaceutical compositions suitable for injectable use include sterile aqueous solutions (where water soluble) or dispersions and sterile powders for the extemporaneous preparation of sterile injectable solutions or dispersions. For intravenous administration, suitable carriers include physiological saline, bacteriostatic water, Cremophor EL (BASF; Parsippany, NJ) or phosphate buffered saline (PBS). In all cases, the composition must be sterile and should be fluid to the extent that easy

syringability exists. It must be stable under the conditions of manufacture and storage and must be preserved against the contaminating action of microorganisms such as bacteria and fungi. The carrier can be a solvent or dispersion medium containing, for example, water, ethanol, polyol (for example, glycerol, propylene glycol, and liquid polyethylene glycol, and the like), and suitable mixtures thereof. The proper fluidity can be maintained, for example, by the use of a coating such as lecithin, by the maintenance of the required particle size in the case of dispersion and by the use of surfactants. Prevention of the action of microorganisms can be achieved by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, ascorbic acid, thimerosal, and the like. In many cases, it will be preferable to include isotonic agents, for example, sugars, polyalcohols such as mannitol, sorbitol, or sodium chloride in the composition. Prolonged absorption of the injectable compositions can be brought about by including in the composition an agent which delays absorption, for example, aluminum monostearate and gelatin.

Sterile injectable solutions can be prepared by incorporating the active compound (*e.g.*, a polypeptide or antibody) in the required amount in an appropriate solvent with one or a combination of ingredients enumerated above, as required, followed by filtered sterilization. Generally, dispersions are prepared by incorporating the active compound into a sterile vehicle which contains a basic dispersion medium, and then incorporating the required other ingredients from those enumerated above. In the case of sterile powders for the preparation of sterile injectable solutions, the preferred methods of preparation are vacuum drying and freeze-drying which yields a powder of the active ingredient plus any additional desired ingredient from a previously sterile-filtered solution thereof.

Oral compositions generally include an inert diluent or an edible carrier. They can be enclosed in gelatin capsules or compressed into tablets. For the purpose of oral therapeutic administration, the active compound can be incorporated with excipients and used in the form of tablets, troches, or capsules. Oral compositions can also be prepared using a fluid carrier for use as a mouthwash, wherein the compound in the fluid carrier is applied orally and swished and expectorated or swallowed.

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Pharmaceutically compatible binding agents, and/or adjuvant materials can be included as part of the composition. The tablets, pills, capsules, troches, and the like can contain any of the following ingredients, or compounds of a similar nature: a binder such as microcrystalline cellulose, gum tragacanth or gelatin; an excipient such as  
5 starch or lactose, a disintegrating agent such as alginic acid, Primogel, or corn starch; a lubricant such as magnesium stearate or Sterotes; a glidant such as colloidal silicon dioxide; a sweetening agent such as sucrose or saccharin; or a flavoring agent such as peppermint, methyl salicylate, or orange flavoring.

For administration by inhalation, the compounds are delivered in the  
10 form of an aerosol spray from a pressurized container or dispenser which contains a suitable propellant, *e.g.*, a gas such as carbon dioxide, or a nebulizer.

Systemic administration can also be by transmucosal or transdermal means. For transmucosal or transdermal administration, penetrants appropriate to the barrier to be permeated are used in the formulation. Such penetrants are generally  
15 known in the art, and include, for example, for transmucosal administration, detergents, bile salts, and fusidic acid derivatives. Transmucosal administration can be accomplished through the use of nasal sprays or suppositories. For transdermal administration, the active compounds are formulated into ointments, salves, gels, or creams as generally known in the art.

20 The compounds can also be prepared in the form of suppositories (*e.g.*, with conventional suppository bases such as cocoa butter and other glycerides) or retention enemas for rectal delivery.

In one embodiment, the active compounds are prepared with carriers that will protect the compound against rapid elimination from the body, such as a controlled  
25 release formulation, including implants and microencapsulated delivery systems. Biodegradable, biocompatible polymers can be used, such as ethylene vinyl acetate, polyanhydrides, polyglycolic acid, collagen, polyorthoesters, and polylactic acid. Methods for preparation of such formulations will be apparent to those skilled in the art. The materials can also be obtained commercially from Alza Corporation and Nova  
30 Pharmaceuticals, Inc. Liposomal suspensions (including liposomes having monoclonal antibodies incorporated therein or thereon) can also be used as pharmaceutically

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acceptable carriers. These can be prepared according to methods known to those skilled in the art, for example, as described in U.S. Patent No. 4,522,811.

It is especially advantageous to formulate oral or parenteral compositions in dosage unit form for ease of administration and uniformity of dosage. Dosage unit  
5 form as used herein refers to physically discrete units suited as unitary dosages for the subject to be treated; each unit containing a predetermined quantity of active compound calculated to produce the desired therapeutic effect in association with the required pharmaceutical carrier. The specification for the dosage unit forms of the invention are dictated by and directly dependent on the unique characteristics of the active compound  
10 and the particular therapeutic effect to be achieved, and the limitations inherent in the art of compounding such an active compound for the treatment of individuals.

For antibodies, the preferred dosage is 0.1 mg/kg to 100 mg/kg of body weight (generally 10 mg/kg to 20 mg/kg). If the antibody is to act in the brain, a dosage of 50 mg/kg to 100 mg/kg is usually appropriate. Generally, partially human antibodies  
15 and fully human antibodies have a longer half-life within the human body than other antibodies. Accordingly, lower dosages and less frequent administration is often possible. Modifications such as lipidation can be used to stabilize antibodies and to enhance uptake and tissue penetration (*e.g.*, into the ovarian epithelium). A method for lipidation of antibodies is described by Cruikshank *et al.* (1997) *J. Acquired Immune*  
20 *Deficiency Syndromes and Human Retrovirology* 14:193.

The invention also provides vaccine compositions for the prevention and/or treatment of ovarian cancer. The invention provides ovarian cancer vaccine compositions in which a protein of a marker of Table 1, or a combination of proteins of the markers of Table 1, are introduced into a subject in order to stimulate an immune  
25 response against the ovarian cancer. The invention also provides ovarian cancer vaccine compositions in which a gene expression construct, which expresses a marker or fragment of a marker identified in Table 1, is introduced into the subject such that a protein or fragment of a protein encoded by a marker of Table 1 is produced by transfected cells in the subject at a higher than normal level and elicits an immune  
30 response.

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In one embodiment, an ovarian cancer vaccine is provided and employed as an immunotherapeutic agent for the prevention of ovarian cancer. In another embodiment, an ovarian cancer vaccine is provided and employed as an immunotherapeutic agent for the treatment of ovarian cancer.

5 By way of example, an ovarian cancer vaccine comprised of the proteins of the markers of Table 1, may be employed for the prevention and/or treatment of ovarian cancer in a subject by administering the vaccine by a variety of routes, *e.g.*, intradermally, subcutaneously, or intramuscularly. In addition, the ovarian cancer vaccine can be administered together with adjuvants and/or immunomodulators to boost  
10 the activity of the vaccine and the subject's response. In one embodiment, devices and/or compositions containing the vaccine, suitable for sustained or intermittent release could be, implanted in the body or topically applied thereto for the relatively slow release of such materials into the body. The ovarian cancer vaccine can be introduced along with immunomodulatory compounds, which can alter the type of immune  
15 response produced in order to produce a response which will be more effective in eliminating the cancer.

In another embodiment, an ovarian cancer vaccine comprised of an expression construct of the markers of Table 1, may be introduced by injection into muscle or by coating onto microprojectiles and using a device designed for the purpose  
20 to fire the projectiles at high speed into the skin. The cells of the subject will then express the protein(s) or fragments of proteins of the markers of Table 1 and induce an immune response. In addition, the ovarian cancer vaccine may be introduced along with expression constructs for immunomodulatory molecules, such as cytokines, which may increase the immune response or modulate the type of immune response produced in  
25 order to produce a response which will be more effective in eliminating the cancer.

The marker nucleic acid molecules of the present invention can also be inserted into vectors and used as gene therapy vectors. Gene therapy vectors can be delivered to a subject by, for example, intravenous injection, local administration (U.S. Patent 5,328,470), or by stereotactic injection (see, *e.g.*, Chen *et al.*, 1994, *Proc. Natl. Acad. Sci. USA* 91:3054-3057).  
30 The pharmaceutical preparation of the gene therapy vector can include the gene therapy vector in an acceptable diluent, or can comprise a slow release matrix in which the gene delivery vehicle is imbedded. Alternatively,

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where the complete gene delivery vector can be produced intact from recombinant cells, e.g. retroviral vectors, the pharmaceutical preparation can include one or more cells which produce the gene delivery system.

The pharmaceutical compositions can be included in a container, pack, or  
5 dispenser together with instructions for administration.

#### V. Predictive Medicine

The present invention pertains to the field of predictive medicine in which diagnostic assays, prognostic assays, pharmacogenomics, and monitoring clinical  
10 trails are used for prognostic (predictive) purposes to thereby treat an individual prophylactically. Accordingly, one aspect of the present invention relates to diagnostic assays for determining the level of expression of one or more marker proteins or nucleic acids, in order to determine whether an individual is at risk of developing ovarian cancer. Such assays can be used for prognostic or predictive purposes to thereby  
15 prophylactically treat an individual prior to the onset of the cancer.

Yet another aspect of the invention pertains to monitoring the influence of agents (e.g., drugs or other compounds administered either to inhibit ovarian cancer or to treat or prevent any other disorder {i.e. in order to understand any ovarian carcinogenic effects that such treatment may have} ) on the expression or activity of a  
20 marker of the invention in clinical trials. These and other agents are described in further detail in the following sections.

#### A. Diagnostic Assays

An exemplary method for detecting the presence or absence of a marker  
25 protein or nucleic acid in a biological sample involves obtaining a biological sample (e.g. an ovary-associated body fluid) from a test subject and contacting the biological sample with a compound or an agent capable of detecting the polypeptide or nucleic acid (e.g., mRNA, genomic DNA, or cDNA). The detection methods of the invention can thus be used to detect mRNA, protein, cDNA, or genomic DNA, for example, in a  
30 biological sample *in vitro* as well as *in vivo*. For example, *in vitro* techniques for detection of mRNA include Northern hybridizations and *in situ* hybridizations. *In vitro* techniques for detection of a marker protein include enzyme linked immunosorbent

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assays (ELISAs), Western blots, immunoprecipitations and immunofluorescence. *In vitro* techniques for detection of genomic DNA include Southern hybridizations. Furthermore, *in vivo* techniques for detection of a marker protein include introducing into a subject a labeled antibody directed against the protein or fragment thereof. For example, the antibody can be labeled with a radioactive marker whose presence and location in a subject can be detected by standard imaging techniques.

A general principle of such diagnostic and prognostic assays involves preparing a sample or reaction mixture that may contain a marker, and a probe, under appropriate conditions and for a time sufficient to allow the marker and probe to interact and bind, thus forming a complex that can be removed and/or detected in the reaction mixture. These assays can be conducted in a variety of ways.

For example, one method to conduct such an assay would involve anchoring the marker or probe onto a solid phase support, also referred to as a substrate, and detecting target marker/probe complexes anchored on the solid phase at the end of the reaction. In one embodiment of such a method, a sample from a subject, which is to be assayed for presence and/or concentration of marker, can be anchored onto a carrier or solid phase support. In another embodiment, the reverse situation is possible, in which the probe can be anchored to a solid phase and a sample from a subject can be allowed to react as an unanchored component of the assay.

There are many established methods for anchoring assay components to a solid phase. These include, without limitation, marker or probe molecules which are immobilized through conjugation of biotin and streptavidin. Such biotinylated assay components can be prepared from biotin-NHS (N-hydroxy-succinimide) using techniques known in the art (*e.g.*, biotinylation kit, Pierce Chemicals, Rockford, IL), and immobilized in the wells of streptavidin-coated 96 well plates (Pierce Chemical). In certain embodiments, the surfaces with immobilized assay components can be prepared in advance and stored.

Other suitable carriers or solid phase supports for such assays include any material capable of binding the class of molecule to which the marker or probe belongs. Well-known supports or carriers include, but are not limited to, glass, polystyrene, nylon, polypropylene, nylon, polyethylene, dextran, amylases, natural and modified celluloses, polyacrylamides, gabbros, and magnetite.

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In order to conduct assays with the above mentioned approaches, the non-immobilized component is added to the solid phase upon which the second component is anchored. After the reaction is complete, uncomplexed components may be removed (*e.g.*, by washing) under conditions such that any complexes formed will remain immobilized upon the solid phase. The detection of marker/probe complexes anchored to the solid phase can be accomplished in a number of methods outlined herein.

In a preferred embodiment, the probe, when it is the unanchored assay component, can be labeled for the purpose of detection and readout of the assay, either directly or indirectly, with detectable labels discussed herein and which are well-known to one skilled in the art.

It is also possible to directly detect marker/probe complex formation without further manipulation or labeling of either component (marker or probe), for example by utilizing the technique of fluorescence energy transfer (see, for example, Lakowicz *et al.*, U.S. Patent No. 5,631,169; Stavrianopoulos, *et al.*, U.S. Patent No. 4,868,103). A fluorophore label on the first, 'donor' molecule is selected such that, upon excitation with incident light of appropriate wavelength, its emitted fluorescent energy will be absorbed by a fluorescent label on a second 'acceptor' molecule, which in turn is able to fluoresce due to the absorbed energy. Alternately, the 'donor' protein molecule may simply utilize the natural fluorescent energy of tryptophan residues. Labels are chosen that emit different wavelengths of light, such that the 'acceptor' molecule label may be differentiated from that of the 'donor'. Since the efficiency of energy transfer between the labels is related to the distance separating the molecules, spatial relationships between the molecules can be assessed. In a situation in which binding occurs between the molecules, the fluorescent emission of the 'acceptor' molecule label in the assay should be maximal. An FET binding event can be conveniently measured through standard fluorometric detection means well known in the art (*e.g.*, using a fluorimeter).

In another embodiment, determination of the ability of a probe to recognize a marker can be accomplished without labeling either assay component (probe or marker) by utilizing a technology such as real-time Biomolecular Interaction Analysis (BIA) (see, *e.g.*, Sjolander, S. and Urbaniczky, C., 1991, *Anal. Chem.* 63:2338-2345

and Szabo *et al.*, 1995, *Curr. Opin. Struct. Biol.* 5:699-705). As used herein, "BIA" or "surface plasmon resonance" is a technology for studying biospecific interactions in real time, without labeling any of the interactants (*e.g.*, BIAcore). Changes in the mass at the binding surface (indicative of a binding event) result in alterations of the refractive index of light near the surface (the optical phenomenon of surface plasmon resonance (SPR)),  
5 resulting in a detectable signal which can be used as an indication of real-time reactions between biological molecules.

Alternatively, in another embodiment, analogous diagnostic and prognostic assays can be conducted with marker and probe as solutes in a liquid phase.  
10 In such an assay, the complexed marker and probe are separated from uncomplexed components by any of a number of standard techniques, including but not limited to: differential centrifugation, chromatography, electrophoresis and immunoprecipitation. In differential centrifugation, marker/probe complexes may be separated from uncomplexed assay components through a series of centrifugal steps, due to the different  
15 sedimentation equilibria of complexes based on their different sizes and densities (see, for example, Rivas, G., and Minton, A.P., 1993, *Trends Biochem Sci.* 18(8):284-7). Standard chromatographic techniques may also be utilized to separate complexed molecules from uncomplexed ones. For example, gel filtration chromatography separates molecules based on size, and through the utilization of an appropriate gel  
20 filtration resin in a column format, for example, the relatively larger complex may be separated from the relatively smaller uncomplexed components. Similarly, the relatively different charge properties of the marker/probe complex as compared to the uncomplexed components may be exploited to differentiate the complex from uncomplexed components, for example through the utilization of ion-exchange  
25 chromatography resins. Such resins and chromatographic techniques are well known to one skilled in the art (see, *e.g.*, Heegaard, N.H., 1998, *J. Mol. Recognit.* Winter 11(1-6):141-8; Hage, D.S., and Tweed, S.A. *J Chromatogr B Biomed Sci Appl* 1997 Oct 10;699(1-2):499-525). Gel electrophoresis may also be employed to separate complexed assay components from unbound components (see, *e.g.*, Ausubel *et al.*, ed.,  
30 *Current Protocols in Molecular Biology*, John Wiley & Sons, New York, 1987-1999). In this technique, protein or nucleic acid complexes are separated based on size or charge, for example. In order to maintain the binding interaction during the

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electrophoretic process, non-denaturing gel matrix materials and conditions in the absence of reducing agent are typically preferred. Appropriate conditions to the particular assay and components thereof will be well known to one skilled in the art.

In a particular embodiment, the level of marker mRNA can be  
5 determined both by *in situ* and by *in vitro* formats in a biological sample using methods known in the art. The term "biological sample" is intended to include tissues, cells, biological fluids and isolates thereof, isolated from a subject, as well as tissues, cells and fluids present within a subject. Many expression detection methods use isolated RNA. For *in vitro* methods, any RNA isolation technique that does not select against the  
10 isolation of mRNA can be utilized for the purification of RNA from ovarian cells (see, e.g., Ausubel *et al.*, ed., *Current Protocols in Molecular Biology*, John Wiley & Sons, New York 1987-1999). Additionally, large numbers of tissue samples can readily be processed using techniques well known to those of skill in the art, such as, for example, the single-step RNA isolation process of Chomczynski (1989, U.S. Patent No.  
15 4,843,155).

The isolated mRNA can be used in hybridization or amplification assays that include, but are not limited to, Southern or Northern analyses, polymerase chain reaction analyses and probe arrays. One preferred diagnostic method for the detection of mRNA levels involves contacting the isolated mRNA with a nucleic acid molecule  
20 (probe) that can hybridize to the mRNA encoded by the gene being detected. The nucleic acid probe can be, for example, a full-length cDNA, or a portion thereof, such as an oligonucleotide of at least 7, 15, 30, 50, 100, 250 or 500 nucleotides in length and sufficient to specifically hybridize under stringent conditions to a mRNA or genomic DNA encoding a marker of the present invention. Other suitable probes for use in the  
25 diagnostic assays of the invention are described herein. Hybridization of an mRNA with the probe indicates that the marker in question is being expressed.

In one format, the mRNA is immobilized on a solid surface and contacted with a probe, for example by running the isolated mRNA on an agarose gel and transferring the mRNA from the gel to a membrane, such as nitrocellulose. In an  
30 alternative format, the probe(s) are immobilized on a solid surface and the mRNA is contacted with the probe(s), for example, in an Affymetrix gene chip array. A skilled

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artisan can readily adapt known mRNA detection methods for use in detecting the level of mRNA encoded by the markers of the present invention.

An alternative method for determining the level of mRNA marker in a sample involves the process of nucleic acid amplification, *e.g.*, by rtPCR (the  
5 experimental embodiment set forth in Mullis, 1987, U.S. Patent No. 4,683,202), ligase chain reaction (Barany, 1991, *Proc. Natl. Acad. Sci. USA*, 88:189-193), self sustained sequence replication (Guatelli *et al.*, 1990, *Proc. Natl. Acad. Sci. USA* 87:1874-1878), transcriptional amplification system (Kwoh *et al.*, 1989, *Proc. Natl. Acad. Sci. USA* 86:1173-1177), Q-Beta Replicase (Lizardi *et al.*, 1988, *Bio/Technology* 6:1197), rolling  
10 circle replication (Lizardi *et al.*, U.S. Patent No. 5,854,033) or any other nucleic acid amplification method, followed by the detection of the amplified molecules using techniques well known to those of skill in the art. These detection schemes are especially useful for the detection of nucleic acid molecules if such molecules are present in very low numbers. As used herein, amplification primers are defined as being  
15 a pair of nucleic acid molecules that can anneal to 5' or 3' regions of a gene (plus and minus strands, respectively, or vice-versa) and contain a short region in between. In general, amplification primers are from about 10 to 30 nucleotides in length and flank a region from about 50 to 200 nucleotides in length. Under appropriate conditions and with appropriate reagents, such primers permit the amplification of a nucleic acid  
20 molecule comprising the nucleotide sequence flanked by the primers.

For *in situ* methods, mRNA does not need to be isolated from the ovarian cells prior to detection. In such methods, a cell or tissue sample is prepared/processed using known histological methods. The sample is then immobilized on a support, typically a glass slide, and then contacted with a probe that can hybridize to mRNA that  
25 encodes the marker.

As an alternative to making determinations based on the absolute expression level of the marker, determinations may be based on the normalized expression level of the marker. Expression levels are normalized by correcting the absolute expression level of a marker by comparing its expression to the expression of a  
30 gene that is not a marker, *e.g.*, a housekeeping gene that is constitutively expressed. Suitable genes for normalization include housekeeping genes such as the actin gene, or epithelial cell-specific genes. This normalization allows the comparison of the

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expression level in one sample, *e.g.*, a patient sample, to another sample, *e.g.*, a non-ovarian cancer sample, or between samples from different sources.

Alternatively, the expression level can be provided as a relative expression level. To determine a relative expression level of a marker, the level of  
5 expression of the marker is determined for 10 or more samples of normal versus cancer cell isolates, preferably 50 or more samples, prior to the determination of the expression level for the sample in question. The mean expression level of each of the genes assayed in the larger number of samples is determined and this is used as a baseline expression level for the marker. The expression level of the marker determined for the  
10 test sample (absolute level of expression) is then divided by the mean expression value obtained for that marker. This provides a relative expression level.

Preferably, the samples used in the baseline determination will be from ovarian cancer or from non-ovarian cancer cells of ovarian tissue. The choice of the cell source is dependent on the use of the relative expression level. Using expression found  
15 in normal tissues as a mean expression score aids in validating whether the marker assayed is ovarian specific (versus normal cells). In addition, as more data is accumulated, the mean expression value can be revised, providing improved relative expression values based on accumulated data. Expression data from ovarian cells provides a means for grading the severity of the ovarian cancer state.

20 In another embodiment of the present invention, a marker protein is detected. A preferred agent for detecting marker protein of the invention is an antibody capable of binding to such a protein or a fragment thereof, preferably an antibody with a detectable label. Antibodies can be polyclonal, or more preferably, monoclonal. An intact antibody, or a fragment or derivatives thereof (*e.g.*, Fab or F(ab')<sub>2</sub>) can be used.  
25 The term "labeled", with regard to the probe or antibody, is intended to encompass direct labeling of the probe or antibody by coupling (*i.e.*, physically linking) a detectable substance to the probe or antibody, as well as indirect labeling of the probe or antibody by reactivity with another reagent that is directly labeled. Examples of indirect labeling include detection of a primary antibody using a fluorescently labeled secondary antibody  
30 and end-labeling of a DNA probe with biotin such that it can be detected with fluorescently labeled streptavidin.

Proteins from ovarian cells can be isolated using techniques that are well known to those of skill in the art. The protein isolation methods employed can, for example, be such as those described in Harlow and Lane (Harlow and Lane, 1988, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York).

A variety of formats can be employed to determine whether a sample contains a protein that binds to a given antibody. Examples of such formats include, but are not limited to, enzyme immunoassay (EIA), radioimmunoassay (RIA), Western blot analysis and enzyme linked immunoabsorbant assay (ELISA). A skilled artisan can readily adapt known protein/antibody detection methods for use in determining whether ovarian cells express a marker of the present invention.

In one format, antibodies, or antibody fragments or derivatives, can be used in methods such as Western blots or immunofluorescence techniques to detect the expressed proteins. In such uses, it is generally preferable to immobilize either the antibody or proteins on a solid support. Suitable solid phase supports or carriers include any support capable of binding an antigen or an antibody. Well-known supports or carriers include glass, polystyrene, polypropylene, polyethylene, dextran, nylon, amylases, natural and modified celluloses, polyacrylamides, gabbros, and magnetite.

One skilled in the art will know many other suitable carriers for binding antibody or antigen, and will be able to adapt such support for use with the present invention. For example, protein isolated from ovarian cells can be run on a polyacrylamide gel electrophoresis and immobilized onto a solid phase support such as nitrocellulose. The support can then be washed with suitable buffers followed by treatment with the detectably labeled antibody. The solid phase support can then be washed with the buffer a second time to remove unbound antibody. The amount of bound label on the solid support can then be detected by conventional means.

The invention also encompasses kits for detecting the presence of a marker protein or nucleic acid in a biological sample (e.g. an ovary-associated body fluid such as a urine sample). Such kits can be used to determine if a subject is suffering from or is at increased risk of developing ovarian cancer. For example, the kit can comprise a labeled compound or agent capable of detecting a marker protein or nucleic acid in a biological sample and means for determining the amount of the protein or

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mRNA in the sample (*e.g.*, an antibody which binds the protein or a fragment thereof, or an oligonucleotide probe which binds to DNA or mRNA encoding the protein). Kits can also include instructions for interpreting the results obtained using the kit.

For antibody-based kits, the kit can comprise, for example: (1) a first  
5 antibody (*e.g.*, attached to a solid support) which binds to a marker protein; and, optionally, (2) a second, different antibody which binds to either the protein or the first antibody and is conjugated to a detectable label.

For oligonucleotide-based kits, the kit can comprise, for example: (1) an oligonucleotide, *e.g.*, a detectably labeled oligonucleotide, which hybridizes to a nucleic  
10 acid sequence encoding a marker protein or (2) a pair of primers useful for amplifying a marker nucleic acid molecule. The kit can also comprise, *e.g.*, a buffering agent, a preservative, or a protein stabilizing agent. The kit can further comprise components necessary for detecting the detectable label (*e.g.*, an enzyme or a substrate). The kit can also contain a control sample or a series of control samples which can be assayed and  
15 compared to the test sample. Each component of the kit can be enclosed within an individual container and all of the various containers can be within a single package, along with instructions for interpreting the results of the assays performed using the kit.

#### B. Pharmacogenomics

20 Agents or modulators which have a stimulatory or inhibitory effect on expression of a marker of the invention can be administered to individuals to treat (prophylactically or therapeutically) ovarian cancer in the patient. In conjunction with such treatment, the pharmacogenomics (*i.e.*, the study of the relationship between an individual's genotype and that individual's response to a foreign compound or drug) of  
25 the individual may be considered. Differences in metabolism of therapeutics can lead to severe toxicity or therapeutic failure by altering the relation between dose and blood concentration of the pharmacologically active drug. Thus, the pharmacogenomics of the individual permits the selection of effective agents (*e.g.*, drugs) for prophylactic or therapeutic treatments based on a consideration of the individual's genotype. Such  
30 pharmacogenomics can further be used to determine appropriate dosages and therapeutic regimens. Accordingly, the level of expression of a marker of the invention in an

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individual can be determined to thereby select appropriate agent(s) for therapeutic or prophylactic treatment of the individual.

Pharmacogenomics deals with clinically significant variations in the response to drugs due to altered drug disposition and abnormal action in affected persons. See, *e.g.*, Linder (1997) *Clin. Chem.* 43(2):254-266. In general, two types of pharmacogenetic conditions can be differentiated. Genetic conditions transmitted as a single factor altering the way drugs act on the body are referred to as "altered drug action." Genetic conditions transmitted as single factors altering the way the body acts on drugs are referred to as "altered drug metabolism". These pharmacogenetic conditions can occur either as rare defects or as polymorphisms. For example, glucose-6-phosphate dehydrogenase (G6PD) deficiency is a common inherited enzymopathy in which the main clinical complication is hemolysis after ingestion of oxidant drugs (antimalarials, sulfonamides, analgesics, nitrofurans) and consumption of fava beans.

As an illustrative embodiment, the activity of drug metabolizing enzymes is a major determinant of both the intensity and duration of drug action. The discovery of genetic polymorphisms of drug metabolizing enzymes (*e.g.*, N-acetyltransferase 2 (NAT 2) and cytochrome P450 enzymes CYP2D6 and CYP2C19) has provided an explanation as to why some patients do not obtain the expected drug effects or show exaggerated drug response and serious toxicity after taking the standard and safe dose of a drug. These polymorphisms are expressed in two phenotypes in the population, the extensive metabolizer (EM) and poor metabolizer (PM). The prevalence of PM is different among different populations. For example, the gene coding for CYP2D6 is highly polymorphic and several mutations have been identified in PM, which all lead to the absence of functional CYP2D6. Poor metabolizers of CYP2D6 and CYP2C19 quite frequently experience exaggerated drug response and side effects when they receive standard doses. If a metabolite is the active therapeutic moiety, a PM will show no therapeutic response, as demonstrated for the analgesic effect of codeine mediated by its CYP2D6-formed metabolite morphine. The other extreme are the so called ultra-rapid metabolizers who do not respond to standard doses. Recently, the molecular basis of ultra-rapid metabolism has been identified to be due to CYP2D6 gene amplification.

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Thus, the level of expression of a marker of the invention in an individual can be determined to thereby select appropriate agent(s) for therapeutic or prophylactic treatment of the individual. In addition, pharmacogenetic studies can be used to apply genotyping of polymorphic alleles encoding drug-metabolizing enzymes to the  
5 identification of an individual's drug responsiveness phenotype. This knowledge, when applied to dosing or drug selection, can avoid adverse reactions or therapeutic failure and thus enhance therapeutic or prophylactic efficiency when treating a subject with a modulator of expression of a marker of the invention.

### 10                    C. Monitoring Clinical Trials

Monitoring the influence of agents (*e.g.*, drug compounds) on the level of expression of a marker of the invention can be applied not only in basic drug screening, but also in clinical trials. For example, the effectiveness of an agent to affect marker expression can be monitored in clinical trials of subjects receiving treatment for ovarian  
15 cancer. In a preferred embodiment, the present invention provides a method for monitoring the effectiveness of treatment of a subject with an agent (*e.g.*, an agonist, antagonist, peptidomimetic, protein, peptide, nucleic acid, small molecule, or other drug candidate) comprising the steps of (i) obtaining a pre-administration sample from a subject prior to administration of the agent; (ii) detecting the level of expression of one  
20 or more selected markers of the invention in the pre-administration sample; (iii) obtaining one or more post-administration samples from the subject; (iv) detecting the level of expression of the marker(s) in the post-administration samples; (v) comparing the level of expression of the marker(s) in the pre-administration sample with the level of expression of the marker(s) in the post-administration sample or samples; and (vi)  
25 altering the administration of the agent to the subject accordingly. For example, increased administration of the agent can be desirable to increase expression of the marker(s) to higher levels than detected, *i.e.*, to increase the effectiveness of the agent. Alternatively, decreased administration of the agent can be desirable to decrease expression of the marker(s) to lower levels than detected, *i.e.*, to decrease the  
30 effectiveness of the agent.

#### D. Electronic Apparatus Readable Media and Arrays

Electronic apparatus readable media comprising a marker of the present invention is also provided. As used herein, "electronic apparatus readable media" refers to any suitable medium for storing, holding or containing data or information that can be  
5 read and accessed directly by an electronic apparatus. Such media can include, but are not limited to: magnetic storage media, such as floppy discs, hard disc storage medium, and magnetic tape; optical storage media such as compact disc; electronic storage media such as RAM, ROM, EPROM, EEPROM and the like; general hard disks and hybrids of these categories such as magnetic/optical storage media. The medium is adapted or  
10 configured for having recorded thereon a marker of the present invention.

As used herein, the term "electronic apparatus" is intended to include any suitable computing or processing apparatus or other device configured or adapted for storing data or information. Examples of electronic apparatus suitable for use with the present invention include stand-alone computing apparatus; networks, including a local  
15 area network (LAN), a wide area network (WAN) Internet, Intranet, and Extranet; electronic appliances such as a personal digital assistants (PDAs), cellular phone, pager and the like; and local and distributed processing systems.

As used herein, "recorded" refers to a process for storing or encoding information on the electronic apparatus readable medium. Those skilled in the art can  
20 readily adopt any of the presently known methods for recording information on known media to generate manufactures comprising the markers of the present invention.

A variety of software programs and formats can be used to store the marker information of the present invention on the electronic apparatus readable medium. For example, the marker nucleic acid sequence can be represented in a word  
25 processing text file, formatted in commercially-available software such as WordPerfect and MicroSoft Word, or represented in the form of an ASCII file, stored in a database application, such as DB2, Sybase, Oracle, or the like, as well as in other forms. Any number of data processor structuring formats (e.g., text file or database) may be employed in order to obtain or create a medium having recorded thereon the the markers  
30 of the present invention.

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By providing the markers of the invention in readable form, one can routinely access the marker sequence information for a variety of purposes. For example, one skilled in the art can use the nucleotide or amino acid sequences of the present invention in readable form to compare a target sequence or target structural motif with the sequence information stored within the data storage means. Search means are used to identify fragments or regions of the sequences of the invention which match a particular target sequence or target motif.

The present invention therefore provides a medium for holding instructions for performing a method for determining whether a subject has ovarian cancer or a pre-disposition to ovarian cancer, wherein the method comprises the steps of determining the presence or absence of a marker and based on the presence or absence of the marker, determining whether the subject has ovarian cancer or a pre-disposition to ovarian cancer and/or recommending a particular treatment for ovarian cancer or pre-ovarian cancer condition.

The present invention further provides in an electronic system and/or in a network, a method for determining whether a subject has ovarian cancer or a pre-disposition to ovarian cancer associated with a marker wherein the method comprises the steps of determining the presence or absence of the marker, and based on the presence or absence of the marker, determining whether the subject has ovarian cancer or a pre-disposition to ovarian cancer, and/or recommending a particular treatment for the ovarian cancer or pre-ovarian cancer condition. The method may further comprise the step of receiving phenotypic information associated with the subject and/or acquiring from a network phenotypic information associated with the subject.

The present invention also provides in a network, a method for determining whether a subject has ovarian cancer or a pre-disposition to ovarian cancer associated with a marker, said method comprising the steps of receiving information associated with the marker receiving phenotypic information associated with the subject, acquiring information from the network corresponding to the marker and/or ovarian cancer, and based on one or more of the phenotypic information, the marker, and the acquired information, determining whether the subject has a ovarian cancer or a pre-disposition to ovarian cancer. The method may further comprise the step of

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recommending a particular treatment for the ovarian cancer or pre-ovarian cancer condition.

The present invention also provides a business method for determining whether a subject has ovarian cancer or a pre-disposition to ovarian cancer, said method  
5 comprising the steps of receiving information associated with the marker, receiving phenotypic information associated with the subject, acquiring information from the network corresponding to the marker and/or ovarian cancer, and based on one or more of the phenotypic information, the marker, and the acquired information, determining whether the subject has ovarian cancer or a pre-disposition to ovarian cancer. The  
10 method may further comprise the step of recommending a particular treatment for the ovarian cancer or pre-ovarian cancer condition.

The invention also includes an array comprising a marker of the present invention. The array can be used to assay expression of one or more genes in the array. In one embodiment, the array can be used to assay gene expression in a tissue to  
15 ascertain tissue specificity of genes in the array. In this manner, up to about 7600 genes can be simultaneously assayed for expression. This allows a profile to be developed showing a battery of genes specifically expressed in one or more tissues.

In addition to such qualitative determination, the invention allows the quantitation of gene expression. Thus, not only tissue specificity, but also the level of  
20 expression of a battery of genes in the tissue is ascertainable. Thus, genes can be grouped on the basis of their tissue expression *per se* and level of expression in that tissue. This is useful, for example, in ascertaining the relationship of gene expression between or among tissues. Thus, one tissue can be perturbed and the effect on gene expression in a second tissue can be determined. In this context, the effect of one cell  
25 type on another cell type in response to a biological stimulus can be determined. Such a determination is useful, for example, to know the effect of cell-cell interaction at the level of gene expression. If an agent is administered therapeutically to treat one cell type but has an undesirable effect on another cell type, the invention provides an assay to determine the molecular basis of the undesirable effect and thus provides the  
30 opportunity to co-administer a counteracting agent or otherwise treat the undesired effect. Similarly, even within a single cell type, undesirable biological effects can be

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determined at the molecular level. Thus, the effects of an agent on expression of other than the target gene can be ascertained and counteracted.

In another embodiment, the array can be used to monitor the time course of expression of one or more genes in the array. This can occur in various biological contexts, as disclosed herein, for example development of ovarian cancer, progression of ovarian cancer, and processes, such a cellular transformation associated with ovarian cancer.

The array is also useful for ascertaining the effect of the expression of a gene on the expression of other genes in the same cell or in different cells. This provides, for example, for a selection of alternate molecular targets for therapeutic intervention if the ultimate or downstream target cannot be regulated.

The array is also useful for ascertaining differential expression patterns of one or more genes in normal and abnormal cells. This provides a battery of genes that could serve as a molecular target for diagnosis or therapeutic intervention.

15

#### E. Surrogate Markers

The markers of the invention may serve as surrogate markers for one or more disorders or disease states or for conditions leading up to disease states, and in particular, ovarian cancer. As used herein, a "surrogate marker" is an objective biochemical marker which correlates with the absence or presence of a disease or disorder, or with the progression of a disease or disorder (*e.g.*, with the presence or absence of a tumor). The presence or quantity of such markers is independent of the disease. Therefore, these markers may serve to indicate whether a particular course of treatment is effective in lessening a disease state or disorder. Surrogate markers are of particular use when the presence or extent of a disease state or disorder is difficult to assess through standard methodologies (*e.g.*, early stage tumors), or when an assessment of disease progression is desired before a potentially dangerous clinical endpoint is reached (*e.g.*, an assessment of cardiovascular disease may be made using cholesterol levels as a surrogate marker, and an analysis of HIV infection may be made using HIV RNA levels as a surrogate marker, well in advance of the undesirable clinical outcomes of myocardial infarction or fully-developed AIDS). Examples of the use of surrogate

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markers in the art include: Koomen *et al.* (2000) *J. Mass. Spectrom.* 35: 258-264; and James (1994) *AIDS Treatment News Archive* 209.

The markers of the invention are also useful as pharmacodynamic markers. As used herein, a "pharmacodynamic marker" is an objective biochemical marker which correlates specifically with drug effects. The presence or quantity of a pharmacodynamic marker is not related to the disease state or disorder for which the drug is being administered; therefore, the presence or quantity of the marker is indicative of the presence or activity of the drug in a subject. For example, a pharmacodynamic marker may be indicative of the concentration of the drug in a biological tissue, in that the marker is either expressed or transcribed or not expressed or transcribed in that tissue in relationship to the level of the drug. In this fashion, the distribution or uptake of the drug may be monitored by the pharmacodynamic marker. Similarly, the presence or quantity of the pharmacodynamic marker may be related to the presence or quantity of the metabolic product of a drug, such that the presence or quantity of the marker is indicative of the relative breakdown rate of the drug *in vivo*. Pharmacodynamic markers are of particular use in increasing the sensitivity of detection of drug effects, particularly when the drug is administered in low doses. Since even a small amount of a drug may be sufficient to activate multiple rounds of marker transcription or expression, the amplified marker may be in a quantity which is more readily detectable than the drug itself. Also, the marker may be more easily detected due to the nature of the marker itself; for example, using the methods described herein, antibodies may be employed in an immune-based detection system for a protein marker, or marker-specific radiolabeled probes may be used to detect a mRNA marker. Furthermore, the use of a pharmacodynamic marker may offer mechanism-based prediction of risk due to drug treatment beyond the range of possible direct observations. Examples of the use of pharmacodynamic markers in the art include: Matsuda *et al.* US 6,033,862; Hattis *et al.* (1991) *Env. Health Perspect.* 90: 229-238; Schentag (1999) *Am. J. Health-Syst. Pharm.* 56 Suppl. 3: S21-S24; and Nicolau (1999) *Am. J. Health-Syst. Pharm.* 56 Suppl. 3: S16-S20.

## VI. Experimental Protocol for all OV markers and M352 - M360

### A. Identification of markers

The markers of the present invention were identified by transcriptional  
5 profiling using mRNA from 9 normal ovarian epithelia, 11 stage I/II ovarian cancer  
tumors and 25 stage III/IV tumors. Clones having expression at least two-fold higher in  
ovarian tumors as compared to their expression in non-ovarian tumor tissues in at least 4  
tumor samples were selected to have their protein-encoding transcript sequences  
determined.

10

### B. Identification of Markers and Assembly of Their Sequences

Clones which displayed an increase in expression in ovarian tumor  
samples over the corresponding average expression of non-tumor samples were used for  
further study. Briefly, BLAST analysis, against both public and proprietary sequence  
15 databases, of EST sequences known to be associated with each clone was performed,  
either directly or in the context of automatically, high-stringency assembled contiguous  
sequences. An identification of protein sequence corresponding to the clone was  
accomplished by obtaining one of the following:

a) a direct match between the protein sequence and at least one EST  
20 sequence in one of its 6 possible translations;

b) a direct match between the nucleotide sequence for the mRNA  
corresponding to the protein sequence and at least one EST sequence;

c) a match between the protein sequence and a contiguous assembly  
(contig) of the EST sequences with other available EST sequences in the databases in  
25 one of its 6 possible translations; or

d) a match between the nucleotide sequence for the mRNA  
corresponding to the protein sequence and a contiguous assembly of the EST sequences  
with other available EST sequences in the databases in one of its 6 possible translations.

C. Identification of Markers Having Newly-Identified Nucleotide and Amino Acid Sequences.

The markers of Table 2 include newly-identified amino acid sequences.

- 5 These sequences were found to be novel based on one of the following criteria:
- a) the protein sequence found within available public databases was incomplete or erroneous, leading to the construction of an additional completed/corrected protein sequence that is not found as such in the public domain;
  - b) based on nucleotide evidence, variants of the protein sequence were
  - 10 additionally constructed that are not found as such in the public domain; or
  - c) the contig for the EST sequences did not match any known protein, so that a novel protein sequence was derived from an open reading frame of the contig.

15 VII. Experimental Protocol for M68, M103, M138, M185, M312, M327-M328, M400, M430-M480, M559, M571-M573, M575-M576, M578-M583, M585-594, and M604-M617

A. Identification of Markers and Assembly of Their Sequences

- 20 The markers of the present invention were identified by transcription profiling using mRNA from 67 ovarian tumors of various histotypes and stage and 96 non-ovarian tumor tissues including normal ovarian epithelium, benign conditions, other normal tissues, and other abnormal tissues. Clones having expression at least three-fold higher in at least 10% of ovarian tumors, as compared to their expression in non-ovarian
- 25 tumor tissue, were designated as ovarian cancer specific markers. These cDNA clones were selected to have their protein-encoding transcript sequences determined. Briefly, BLAST analysis, against both public and proprietary sequence databases, of EST sequences known to be associated with each clone was performed, either directly or in the context of automatically, high-stringency assembled contiguous sequences. An
- 30 identification of protein sequence corresponding to the clone was accomplished by obtaining one of the following:
- a) a direct match between the protein sequence and at least one EST sequence in one of its 6 possible translations;

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b) a direct match between the nucleotide sequence for the mRNA corresponding to the protein sequence and at least one EST sequence;

c) a match between the protein sequence and a contiguous assembly (contig) of the EST sequences with other available EST sequences in the databases in one of its 6 possible translations; or

d) a match between the nucleotide sequence for the mRNA corresponding to the protein sequence and a contiguous assembly of the EST sequences with other available EST sequences in the databases in one of its 6 possible translations.

10                    B. Identification of Markers Having Newly-Identified Amino Acid Sequences.

The markers of Table 2 include newly-identified amino acid sequences. These sequences were found to be novel based on one of the following criteria:

- a) the protein sequence found within available public databases was incomplete or erroneous, leading to the construction of an additional completed/corrected protein sequence that is not found as such in the public domain;
- b) based on nucleotide evidence, variants of the protein sequence were additionally constructed that are not found as such in the public domain; or
- c) the contig for the EST sequences did not match any known protein, so that a novel protein sequence was derived from an open reading frame of the contig.

VIII. Gene Expression Analysis

Total RNA from normal human tissue was obtained from commercial sources. The integrity of the RNA was verified by agarose gel electrophoresis and ethidium bromide staining. Cell lines were purchased from ATCC and grown under the conditions recommended by ATCC. Total RNA from a number of various cell lines was prepared using commercial kits (Qiagen). First strand cDNA was prepared using oligo-dT primer and standard conditions. Each RNA preparation was treated with DNase I (Ambion) at 37°C for 1 hour.

Novel gene expression was measured by TaqMan<sup>®</sup> quantitative PCR (Perkin Elmer Applied Biosystems) in cDNA prepared from the following normal human tissues: heart, kidney, skeletal muscle, pancreas, skin, dorsal root ganglion,

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breast, ovary, prostate, salivary glands, lung, colon, liver and lymph node. Figure 1 graphically represents the results of the TaqMan® expression study. The columns labelled A to V depict the expression level observed for OV88 in the following tissues:

- Column A: Heart, normal tissue
- 5 Column B: Heart, CHF tissue
- Column C: Kidney, normal tissue
- Column D: Skeletal muscle, normal tissue
- Column E: Pancreas, normal tissue
- Column F: Skin, normal tissue
- 10 Column G: Dorsal root, normal tissue
- Column H: Breast, normal tissue
- Column I: Breast, tumor tissue
- Column J: Ovary, normal tissue
- Column K: Ovary, tumor tissue
- 15 Column L: Prostate, normal tissue
- Column M: Prostate, tumor tissue
- Column N: Salivary glands, normal tissue
- Column O: Lung, normal tissue
- Column P: Lung, tumor tissue
- 20 Column Q: Lung, COPD tissue
- Column R: Colon, IBD tissue
- Column S: Liver, normal tissue
- Column T: Liver fibrosis
- Column U: Lymph node, normal tissue
- 25 Column V: Positive control

#### IX. Summary of the Data Provided in the Tables

Tables 1-3 list the markers of the present invention. In the Tables the markers are identified with a name ("Marker"), the name the gene is commonly known  
 30 by, if applicable ("Gene Name"), the Sequence Listing identifier of the cDNA sequence of a nucleotide transcript encoded by or corresponding to the marker ("SEQ ID NO (nts)"), the Sequence Listing identifier of the amino acid sequence of a protein encoded

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by the nucleotide transcript ("SEQ ID NO (AAs)"), and the location of the protein coding sequence within the cDNA sequence ("CDS").

Table 1 lists all of the markers of the invention, which are over-expressed in ovarian cancer cells compared to normal (*i.e.*, non-cancerous) ovarian cells and  
5 comprises markers listed in Tables 2 and 3. Table 2 lists newly-identified nucleotide and amino acid sequences useful as ovarian cancer markers. Table 3 lists newly-identified nucleotide sequences useful as ovarian cancer markers.

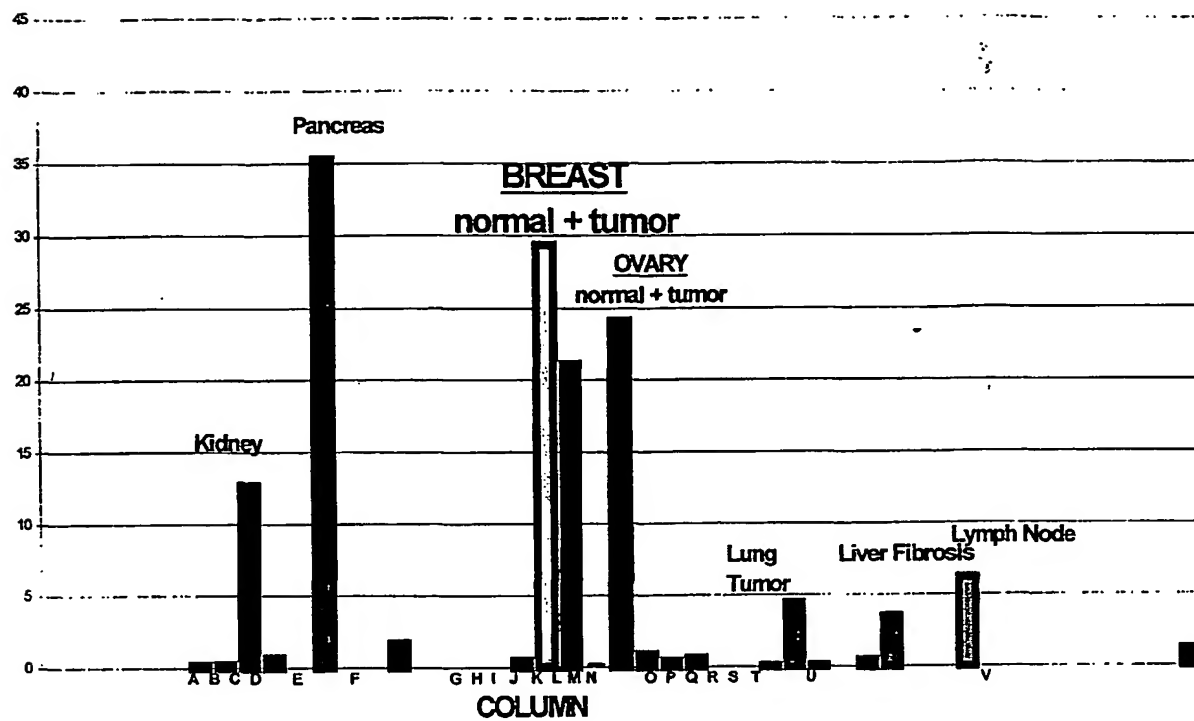
#### Other Embodiments

10 Those skilled in the art will recognize, or be able to ascertain using no more than routine experimentation, many equivalents to the specific embodiments of the invention described herein. Such equivalents are intended to be encompassed by the following claims:

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What is claimed:

1. A method of assessing whether a patient is afflicted with ovarian cancer, the method comprising comparing:
  - 5           a) the level of expression of a marker in a patient sample, wherein the marker is selected from Table 1, and
  - b) the normal level of expression of the marker in a control non-ovarian cancer sample,wherein a significant increase in the level of expression of the marker in  
10   the patient sample and the normal level is an indication that the patient is afflicted with ovarian cancer.

**Figure 1**

## SEQUENCE LISTING

<110> Millennium Pharmaceuticals, Inc. et al.

<120> Nucleic Acid Molecules and Proteins For The Identification,  
Assessment, Prevention, and Therapy of Ovarian Cancer

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<150> 60/276,025

<151> 2001-03-14

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<212> DNA

<213> Homo sapiens

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<210> 2

<211> 1279

<212> PRT

<213> Homo sapiens

<400> 2

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			20				25					30			
Thr	Val	Ser	Val	Phe	Ser	Met	Phe	Arg	Tyr	Ser	Asn	Trp	Leu	Asp	Lys
		35					40					45			
Leu	Tyr	Met	Val	Val	Gly	Thr	Leu	Ala	Ala	Ile	Ile	His	Gly	Ala	Gly
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Leu	Pro	Leu	Met	Met	Leu	Val	Phe	Gly	Glu	Met	Thr	Asp	Ile	Phe	Ala
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Asn	Ala	Gly	Asn	Leu	Glu	Asp	Leu	Met	Ser	Asn	Ile	Thr	Asn	Arg	Ser
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Asp	Ile	Asn	Asp	Thr	Gly	Phe	Phe	Met	Asn	Leu	Glu	Glu	Asp	Met	Thr
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Arg	Tyr	Ala	Tyr	Tyr	Tyr	Ser	Gly	Ile	Gly	Ala	Gly	Val	Leu	Val	Ala
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Ala	Tyr	Ile	Gln	Val	Ser	Phe	Trp	Cys	Leu	Ala	Ala	Gly	Arg	Gln	Ile
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His	Lys	Ile	Arg	Lys	Gln	Phe	Phe	His	Ala	Ile	Met	Arg	Gln	Glu	Ile
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Gly	Trp	Phe	Asp	Val	His	Asp	Val	Gly	Glu	Leu	Asn	Thr	Arg	Leu	Thr
			165					170						175	
Asp	Asp	Val	Ser	Lys	Ile	Asn	Glu	Gly	Ile	Gly	Asp	Lys	Ile	Gly	Met
			180					185					190		
Phe	Phe	Gln	Ser	Met	Ala	Thr	Phe	Phe	Thr	Gly	Phe	Ile	Val	Gly	Phe
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Asp	Lys	Glu	Leu	Leu	Ala	Tyr	Ala	Lys	Ala	Gly	Ala	Val	Ala	Glu	Glu
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Val	Leu	Ala	Ala	Ile	Arg	Thr	Val	Ile	Ala	Phe	Gly	Gly	Gln	Lys	Lys
			260					265					270		
Glu	Leu	Glu	Arg	Tyr	Asn	Lys	Asn	Leu	Glu	Glu	Ala	Lys	Arg	Ile	Gly
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Leu	Ile	Tyr	Ala	Ser	Tyr	Ala	Leu	Ala	Phe	Trp	Tyr	Gly	Thr	Thr	Leu
305					310					315					320
Val	Leu	Ser	Gly	Glu	Tyr	Ser	Ile	Gly	Gln	Val	Leu	Thr	Val	Phe	Ser
			325						330					335	
Val	Leu	Ile	Gly	Ala	Phe	Ser	Val	Gly	Gln	Ala	Ser	Pro	Ser	Ile	Glu
			340					345					350		
Ala	Phe	Ala	Asn	Ala	Arg	Gly	Ala	Ala	Tyr	Glu	Ile	Phe	Lys	Ile	Ile
	355						360					365			
Asp	Asn	Lys	Pro	Ser	Ile	Asp	Ser	Tyr	Ser	Lys	Ser	Gly	His	Lys	Pro
	370					375					380				

Asp	Asn	Ile	Lys	Gly	Asn	Leu	Glu	Phe	Arg	Asn	Val	His	Phe	Ser	Tyr	385	390	395	400
Pro	Ser	Arg	Lys	Glu	Val	Lys	Ile	Leu	Lys	Gly	Leu	Asn	Leu	Lys	Val	405	410		415
Gln	Ser	Gly	Gln	Thr	Val	Ala	Leu	Val	Gly	Asn	Ser	Gly	Cys	Gly	Lys	420	425		430
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Met	Val	Ser	Val	Asp	Gly	Gln	Asp	Ile	Arg	Thr	Ile	Asn	Val	Arg	Phe	450	455		460
Leu	Arg	Glu	Ile	Ile	Gly	Val	Val	Ser	Gln	Glu	Pro	Val	Leu	Phe	Ala	465	470		480
Thr	Thr	Ile	Ala	Glu	Asn	Ile	Arg	Tyr	Gly	Arg	Glu	Asn	Val	Thr	Met	485	490		495
Asp	Glu	Ile	Glu	Lys	Ala	Val	Lys	Glu	Ala	Asn	Ala	Tyr	Asp	Phe	Ile	500	505		510
Met	Lys	Leu	Pro	His	Lys	Phe	Asp	Thr	Leu	Val	Gly	Glu	Arg	Gly	Ala	515	520		525
Gln	Leu	Ser	Gly	Gly	Gln	Lys	Gln	Arg	Ile	Ala	Ile	Ala	Arg	Ala	Leu	530	535		540
Val	Arg	Asn	Pro	Lys	Ile	Leu	Leu	Leu	Asp	Glu	Ala	Thr	Ser	Ala	Leu	545	550		560
Asp	Thr	Glu	Ser	Glu	Ala	Val	Val	Gln	Val	Ala	Leu	Asp	Lys	Ala	Arg	565	570		575
Lys	Gly	Arg	Thr	Thr	Ile	Val	Ile	Ala	His	Arg	Leu	Ser	Thr	Val	Arg	580	585		590
Asn	Ala	Asp	Val	Ile	Ala	Gly	Phe	Asp	Asp	Gly	Val	Ile	Val	Glu	Lys	595	600		605
Gly	Asn	His	Asp	Glu	Leu	Met	Lys	Glu	Lys	Gly	Ile	Tyr	Phe	Lys	Leu	610	615		620
Val	Thr	Met	Gln	Thr	Ala	Gly	Asn	Glu	Val	Glu	Leu	Glu	Asn	Ala	Ala	625	630		640
Asp	Glu	Ser	Lys	Ser	Glu	Ile	Asp	Ala	Leu	Glu	Met	Ser	Ser	Asn	Asp	645	650		655
Ser	Arg	Ser	Ser	Leu	Ile	Arg	Lys	Arg	Ser	Thr	Arg	Arg	Ser	Val	Arg	660	665		670
Gly	Ser	Gln	Ala	Gln	Asp	Arg	Lys	Leu	Ser	Thr	Lys	Glu	Ala	Leu	Asp	675	680		685
Glu	Ser	Ile	Pro	Pro	Val	Ser	Phe	Trp	Arg	Ile	Met	Lys	Leu	Asn	Leu	690	695		700
Thr	Glu	Trp	Pro	Tyr	Phe	Val	Val	Gly	Val	Phe	Cys	Ala	Ile	Ile	Asn	705	710		720
Gly	Gly	Leu	Gln	Pro	Ala	Phe	Ala	Ile	Ile	Phe	Ser	Lys	Ile	Ile	Gly	725	730		735
Val	Phe	Thr	Arg	Ile	Asp	Asp	Pro	Glu	Thr	Lys	Arg	Gln	Asn	Ser	Asn	740	745		750
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Phe	Phe	Leu	Gln	Gly	Phe	Thr	Phe	Gly	Lys	Ala	Gly	Glu	Ile	Leu	Thr	770	775		780
Lys	Arg	Leu	Arg	Tyr	Met	Val	Phe	Arg	Ser	Met	Leu	Arg	Gln	Asp	Val	785	790		800
Ser	Trp	Phe	Asp	Asp	Pro	Lys	Asn	Thr	Thr	Gly	Ala	Leu	Thr	Thr	Arg	805	810		815
Leu	Ala	Asn	Asp	Ala	Ala	Gln	Val	Lys	Gly	Ala	Ile	Gly	Ser	Arg	Leu	820	825		830
Ala	Val	Ile	Thr	Gln	Asn	Ile	Ala	Asn	Leu	Gly	Thr	Gly	Ile	Ile	Ile	835	840		845

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&lt;210&gt; 3

&lt;211&gt; 3859

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 3

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&lt;210&gt; 4

&lt;211&gt; 1014

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 4

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50          55          60
Arg His Pro Asp Val Glu Val Asp Gly Phe Ser Glu Leu Arg Trp Asp
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Asp Gln Gln Lys Val Lys Lys Thr Ala Glu Ala Gly Gly Val Thr Gly
85          90          95
Lys Gly Gln Asp Gly Ile Gly Ser Lys Ala Glu Lys Thr Leu Gly Asp
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Phe Ala Ala Glu Tyr Ala Lys Ser Asn Arg Ser Thr Cys Lys Gly Cys
115         120         125
Met Glu Lys Ile Glu Lys Gly Gln Val Arg Leu Ser Lys Lys Met Val
130         135         140
Asp Pro Glu Lys Pro Gln Leu Gly Met Ile Asp Arg Trp Tyr His Pro
145         150         155         160
Gly Cys Phe Val Lys Asn Arg Glu Glu Leu Gly Phe Arg Pro Glu Tyr
165         170         175
Ser Ala Ser Gln Leu Lys Gly Phe Ser Leu Leu Ala Thr Glu Asp Lys
180         185         190
Glu Ala Leu Lys Lys Gln Leu Pro Gly Val Lys Ser Glu Gly Lys Arg
195         200         205
Lys Gly Asp Glu Val Asp Gly Val Asp Glu Val Ala Lys Lys Lys Ser
210         215         220
Lys Lys Glu Lys Asp Lys Asp Ser Lys Leu Glu Lys Ala Leu Lys Ala
225         230         235         240
Gln Asn Asp Leu Ile Trp Asn Ile Lys Asp Glu Leu Lys Lys Val Cys
245         250         255
Ser Thr Asn Asp Leu Lys Glu Leu Leu Ile Phe Asn Lys Gln Gln Val
260         265         270
Pro Ser Gly Glu Ser Ala Ile Leu Asp Arg Val Ala Asp Gly Met Val
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Lys Ser Asp Ala Tyr Tyr Cys Thr Gly Asp Val Thr Ala Trp Thr Lys
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 Lys Glu Phe Arg Glu Ile Ser Tyr Leu Lys Lys Leu Lys Val Lys Lys  
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 Gln Asp Arg Ile Phe Pro Pro Glu Thr Ser Ala Ser Val Ala Ala Thr  
 355 360 365  
 Pro Pro Pro Ser Thr Ala Ser Ala Pro Ala Ala Val Asn Ser Ser Ala  
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 385 390 395 400  
 Leu Ser Arg Asn Lys Asp Glu Val Lys Ala Met Ile Glu Lys Leu Gly  
 405 410 415  
 Gly Lys Leu Thr Gly Thr Ala Asn Lys Ala Ser Leu Cys Ile Ser Thr  
 420 425 430  
 Lys Lys Glu Val Glu Lys Met Asn Lys Lys Met Glu Glu Val Lys Glu  
 435 440 445  
 Ala Asn Ile Arg Val Val Ser Glu Asp Phe Leu Gln Asp Val Ser Ala  
 450 455 460  
 Ser Thr Lys Ser Leu Gln Glu Leu Phe Leu Ala His Ile Leu Ser Pro  
 465 470 475 480  
 Trp Gly Ala Glu Val Lys Ala Glu Pro Val Glu Val Val Ala Pro Arg  
 485 490 495  
 Gly Lys Ser Gly Ala Ala Leu Ser Lys Lys Ser Lys Gly Gln Val Lys  
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 Glu Glu Gly Ile Asn Lys Ser Glu Lys Arg Met Lys Leu Thr Leu Lys  
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 Ser Gln Gly Ser Ser Asp Ser Gln Ile Leu Asp Leu Ser Asn Arg Phe  
 725 730 735  
 Tyr Thr Leu Ile Pro His Asp Phe Gly Met Lys Lys Pro Pro Leu Leu  
 740 745 750  
 Asn Asn Ala Asp Ser Val Gln Ala Lys Val Glu Met Leu Asp Asn Leu  
 755 760 765  
 Leu Asp Ile Glu Val Ala Tyr Ser Leu Leu Arg Gly Gly Ser Asp Asp  
 770 775 780

Ser Ser Lys Asp Pro Ile Asp Val Asn Tyr Glu Lys Leu Lys Thr Asp  
 785 790 795 800  
 Ile Lys Val Val Asp Arg Asp Ser Glu Glu Ala Glu Ile Ile Arg Lys  
 805 810 815  
 Tyr Val Lys Asn Thr His Ala Thr Thr His Ser Ala Tyr Asp Leu Glu  
 820 825 830  
 Val Ile Asp Ile Phe Lys Ile Glu Arg Glu Gly Glu Cys Gln Arg Tyr  
 835 840 845  
 Lys Pro Phe Lys Gln Leu His Asn Arg Arg Leu Leu Trp His Gly Ser  
 850 855 860  
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 Pro Pro Glu Ala Pro Val Thr Gly Tyr Met Phe Gly Lys Gly Ile Tyr  
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 Gly Asp Pro Ile Gly Leu Ile Leu Leu Gly Glu Val Ala Leu Gly Asn  
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 Met Tyr Glu Leu Lys His Ala Ser His Ile Ser Arg Leu Pro Lys Gly  
 930 935 940  
 Lys His Ser Val Lys Gly Leu Gly Lys Thr Thr Pro Asp Pro Ser Ala  
 945 950 955 960  
 Asn Ile Ser Leu Asp Gly Val Asp Val Pro Leu Gly Thr Gly Ile Ser  
 965 970 975  
 Ser Gly Val Ile Asp Thr Ser Leu Leu Tyr Asn Glu Tyr Ile Val Tyr  
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 Phe Lys Thr Ser Leu Trp  
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 <211> 1465  
 <212> DNA  
 <213> Homo sapiens

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 gcgggatgct ttgaacattg aaacagccat caagaccaa ggtgtggatg aggtcaccat 300  
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 gagaaggacc aaaaaggaac ttgcatcagc actgaagtca gccttatctg gccacctgga 420  
 gacggtgatt ttgggcctat tgaagacacc tgctcagtat gacgcttctg agctaaaaagc 480  
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&lt;210&gt; 6

&lt;211&gt; 339

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 6

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His Ser Thr Pro Pro Ser Ala Tyr Gly Ser Val Lys Ala Tyr Thr Asn
      20          25          30
Phe Asp Ala Glu Arg Asp Ala Leu Asn Ile Glu Thr Ala Ile Lys Thr
      35          40          45
Lys Gly Val Asp Glu Val Thr Ile Val Asn Ile Leu Thr Asn Arg Ser
      50          55          60
Asn Ala Gln Arg Gln Asp Ile Ala Phe Ala Tyr Gln Arg Arg Thr Lys
      65          70          75          80
Lys Glu Leu Ala Ser Ala Leu Lys Ser Ala Leu Ser Gly His Leu Glu
      85          90          95
Thr Val Ile Leu Gly Leu Leu Lys Thr Pro Ala Gln Tyr Asp Ala Ser
      100          105          110
Glu Leu Lys Ala Ser Met Lys Gly Leu Gly Thr Asp Glu Asp Ser Leu
      115          120          125
Ile Glu Ile Ile Cys Ser Arg Thr Asn Gln Glu Leu Gln Glu Ile Asn
      130          135          140
Arg Val Tyr Lys Glu Met Tyr Lys Thr Asp Leu Glu Lys Asp Ile Ile
      145          150          155          160
Ser Asp Thr Ser Gly Asp Phe Arg Lys Leu Met Val Ala Leu Ala Lys
      165          170          175
Gly Arg Arg Ala Glu Asp Gly Ser Val Ile Asp Tyr Glu Leu Ile Asp
      180          185          190
Gln Asp Ala Arg Asp Leu Tyr Asp Ala Gly Val Lys Arg Lys Gly Thr
      195          200          205
Asp Val Pro Lys Trp Ile Ser Ile Met Thr Glu Arg Ser Val Pro His
      210          215          220
Leu Gln Lys Val Phe Asp Arg Tyr Lys Ser Tyr Ser Pro Tyr Asp Met
      225          230          235          240
Leu Glu Ser Ile Arg Lys Glu Val Lys Gly Asp Leu Glu Asn Ala Phe
      245          250          255
Leu Asn Leu Val Gln Cys Ile Gln Asn Lys Pro Leu Tyr Phe Ala Asp
      260          265          270
Arg Leu Tyr Asp Ser Met Lys Gly Lys Gly Thr Arg Asp Lys Val Leu
      275          280          285
Ile Arg Ile Met Val Ser Arg Ser Glu Val Asp Met Leu Lys Ile Arg
      290          295          300
Ser Glu Phe Lys Arg Lys Tyr Gly Lys Ser Leu Tyr Tyr Tyr Ile Gln
      305          310          315          320
Gln Asp Thr Lys Gly Asp Tyr Gln Lys Ala Leu Leu Tyr Leu Cys Gly
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Gly Asp Asp

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 <211> 1362  
 <212> DNA  
 <213> Homo sapiens

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 tgggtctgtc aaagcctata ctaactttga tgctgagcgg gatgctttga acattgaaac 180  
 agccatcaag accaaagggt tggatgaggt caccattgtc aacattttga ccaaccgcag 240  
 caatgcacag agacaggata ttgccttcgc ctaccagaga aggacaaaaa aggaacttgc 300  
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<210> 8  
 <211> 339  
 <212> PRT  
 <213> Homo sapiens

<400> 8  
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 Phe Asp Ala Glu Arg Asp Ala Leu Asn Ile Glu Thr Ala Ile Lys Thr  
 35 40 45  
 Lys Gly Val Asp Glu Val Thr Ile Val Asn Ile Leu Thr Asn Arg Ser  
 50 55 60  
 Asn Ala Gln Arg Gln Asp Ile Ala Phe Ala Tyr Gln Arg Arg Thr Lys  
 65 70 75 80  
 Lys Glu Leu Ala Ser Ala Leu Lys Ser Ala Leu Ser Gly His Leu Glu  
 85 90 95  
 Thr Val Ile Leu Gly Leu Leu Lys Thr Pro Ala Gln Tyr Asp Ala Ser  
 100 105 110  
 Glu Leu Lys Ala Ser Met Lys Gly Leu Gly Thr Asp Glu Asp Ser Leu  
 115 120 125  
 Ile Glu Ile Ile Cys Ser Arg Thr Asn Gln Glu Leu Gln Glu Ile Asn  
 130 135 140  
 Arg Val Tyr Lys Glu Met Tyr Lys Thr Asp Leu Glu Lys Asp Ile Ile  
 145 150 155 160  
 Ser Asp Thr Ser Gly Asp Phe Arg Lys Leu Met Val Ala Leu Ala Lys  
 165 170 175

Gly Arg Arg Ala Glu Asp Gly Ser Val Ile Asp Tyr Glu Leu Ile Asp  
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 Gln Asp Ala Arg Asp Leu Tyr Asp Ala Gly Val Lys Arg Lys Gly Thr  
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 Asp Val Pro Lys Trp Ile Ser Ile Met Thr Glu Arg Ser Val Pro His  
                   210                  215                  220  
 Leu Gln Lys Val Phe Asp Arg Tyr Lys Ser Tyr Ser Pro Tyr Asp Met  
 225                  230                  235                  240  
 Leu Glu Ser Ile Arg Lys Glu Val Lys Gly Asp Leu Glu Asn Ala Phe  
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 Leu Asn Leu Val Gln Cys Ile Gln Asn Lys Pro Leu Tyr Phe Ala Asp  
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 Arg Leu Tyr Asp Ser Met Lys Gly Lys Gly Thr Arg Asp Lys Val Leu  
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 Ile Arg Ile Met Val Ser Arg Ser Glu Val Asp Met Leu Lys Ile Arg  
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 Ser Glu Phe Lys Arg Lys Tyr Gly Lys Ser Leu Tyr Tyr Tyr Ile Gln  
 305                  310                  315                  320  
 Gln Asp Thr Lys Gly Asp Tyr Gln Lys Ala Leu Leu Tyr Leu Cys Gly  
                   325                  330                  335  
 Gly Asp Asp

&lt;210&gt; 9

&lt;211&gt; 1982

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 9

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tgtgctaaaa atacttttta aaatcaattt tgttgattgt agtaatttct atttgactg 1920
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gt 1982

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&lt;210&gt; 10

&lt;211&gt; 321

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 10

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  20          25          30
Gly Thr Asp Glu Asp Ala Ile Ile Ser Val Leu Ala Tyr Arg Asn Thr
  35          40          45
Ala Gln Arg Gln Glu Ile Arg Thr Ala Tyr Lys Ser Thr Ile Gly Arg
  50          55          60
Asp Leu Ile Asp Asp Leu Lys Ser Glu Leu Ser Gly Asn Phe Glu Gln
  65          70          75          80
Val Ile Val Gly Met Met Thr Pro Thr Val Leu Tyr Asp Val Gln Glu
  85          90          95
Leu Arg Arg Ala Met Lys Gly Ala Gly Thr Asp Glu Gly Cys Leu Ile
  100         105         110
Glu Ile Leu Ala Ser Arg Thr Pro Glu Glu Ile Arg Arg Ile Ser Gln
  115         120         125
Thr Tyr Gln Gln Gln Tyr Gly Arg Ser Leu Glu Asp Asp Ile Arg Ser
  130         135         140
Asp Thr Ser Phe Met Phe Gln Arg Val Leu Val Ser Leu Ser Ala Gly
  145         150         155         160
Gly Arg Asp Glu Gly Asn Tyr Leu Asp Asp Ala Leu Val Arg Gln Asp
  165         170         175
Ala Gln Asp Leu Tyr Glu Ala Gly Glu Lys Lys Trp Gly Thr Asp Glu
  180         185         190
Val Lys Phe Leu Thr Val Leu Cys Ser Arg Asn Arg Asn His Leu Leu
  195         200         205
His Val Phe Asp Glu Tyr Lys Arg Ile Ser Gln Lys Asp Ile Glu Gln
  210         215         220
Ser Ile Lys Ser Glu Thr Ser Gly Ser Phe Glu Asp Ala Leu Leu Ala
  225         230         235         240
Ile Val Lys Cys Met Arg Asn Lys Ser Ala Tyr Phe Ala Glu Lys Leu
  245         250         255
Tyr Lys Ser Met Lys Gly Leu Gly Thr Asp Asp Asn Thr Leu Ile Arg
  260         265         270
Val Met Val Ser Arg Ala Glu Ile Asp Met Leu Asp Ile Arg Ala His
  275         280         285
Phe Lys Arg Leu Tyr Gly Lys Ser Leu Tyr Ser Phe Ile Lys Gly Asp
  290         295         300
Thr Ser Gly Asp Tyr Arg Lys Val Leu Leu Val Leu Cys Gly Gly Asp
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Asp

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&lt;210&gt; 11

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 <212> DNA  
 <213> Homo sapiens

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 <211> 265  
 <212> PRT  
 <213> Homo sapiens

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 Leu Lys Trp Pro Ser Ala Leu Pro Thr Ile Leu Gln Ile Ala Leu Ala  
 35 40 45  
 Phe Gly Leu Ala Ile Gly Thr Leu Ala Gln Ala Leu Gly Pro Val Ser  
 50 55 60  
 Gly Gly His Ile Asn Pro Ala Ile Thr Leu Ala Leu Leu Val Gly Asn  
 65 70 75 80  
 Gln Ile Ser Leu Leu Arg Ala Phe Phe Tyr Val Ala Ala Gln Leu Val  
 85 90 95  
 Gly Ala Ile Ala Gly Ala Gly Ile Leu Tyr Gly Val Ala Pro Leu Asn  
 100 105 110  
 Ala Arg Gly Asn Leu Ala Val Asn Ala Leu Asn Asn Asn Thr Thr Gln  
 115 120 125  
 Gly Gln Ala Met Val Val Glu Leu Ile Leu Thr Phe Gln Leu Ala Leu  
 130 135 140  
 Cys Ile Phe Ala Ser Thr Asp Ser Arg Arg Thr Ser Pro Val Gly Ser  
 145 150 155 160  
 Pro Ala Leu Ser Ile Gly Leu Ser Val Thr Leu Gly His Leu Val Gly  
 165 170 175  
 Ile Tyr Phe Thr Gly Cys Ser Met Asn Pro Ala Arg Ser Phe Gly Pro  
 180 185 190

15

Ala Val Val Met Asn Arg Phe Ser Pro Ala His Trp Val Phe Trp Val  
 195 200 205  
 Gly Pro Ile Val Gly Ala Val Leu Ala Ala Ile Leu Tyr Phe Tyr Leu  
 210 215 220  
 Leu Phe Pro Asn Ser Leu Ser Leu Ser Glu Arg Val Ala Ile Ile Lys  
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 Gly Thr Tyr Glu Pro Asp Glu Asp Trp Glu Glu Gln Arg Glu Glu Arg  
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 Lys Lys Thr Met Glu Leu Thr Thr Arg  
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<210> 13  
 <211> 1653  
 <212> DNA  
 <213> Homo. sapiens

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<210> 14  
 <211> 464  
 <212> PRT  
 <213> Homo sapiens

<400> 14  
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 Val Ala Arg His Gly Ile Leu Gln Val Ala Gly Asp Asp Arg Phe Gly  
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		35					40				45				
Leu	Asp	His	Gln	Arg	Leu	Leu	Glu	Tyr	Leu	Lys	Tyr	Thr	Leu	Asp	Gln
	50					55					60				
Tyr	Val	Glu	Asn	Asp	Tyr	Thr	Ile	Val	Tyr	Phe	His	Tyr	Gly	Leu	Asn
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Phe	Asp	Arg	Lys	Asp	Gly	Asp	Leu	Thr	Met	Trp	Pro	Arg	Leu	Val	Ser
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Asp	Tyr	Arg	Tyr	Lys	Lys	Asn	Leu	Lys	Ala	Leu	Tyr	Val	Val	His	Pro
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Thr	Ser	Phe	Ile	Lys	Val	Leu	Trp	Asn	Ile	Leu	Lys	Pro	Leu	Ile	Ser
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His	Lys	Phe	Gly	Lys	Lys	Val	Ile	Tyr	Phe	Asn	Tyr	Leu	Ser	Glu	Leu
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His	Glu	His	Leu	Lys	Tyr	Asp	Gln	Leu	Val	Ile	Pro	Pro	Glu	Val	Leu
			180					185					190		
Arg	Tyr	Asp	Glu	Lys	Leu	Gln	Ser	Leu	His	Glu	Gly	Arg	Thr	Pro	Pro
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Pro	Thr	Lys	Thr	Pro	Pro	Pro	Arg	Pro	Pro	Leu	Pro	Thr	Gln	Gln	Phe
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Pro	Pro	Val	Leu	Arg	Phe	Thr	Val	Thr	Tyr	Leu	Arg	Glu	Lys	Gly	Leu
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Arg	Thr	Glu	Gly	Leu	Phe	Arg	Arg	Ser	Ala	Ser	Val	Gln	Thr	Val	Arg
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Glu	Leu	Pro	Gln	Pro	Leu	Leu	Thr	Phe	Gln	Ala	Tyr	Glu	Gln	Ile	Leu
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Gly	Ile	Thr	Cys	Val	Glu	Ser	Ser	Leu	Arg	Val	Thr	Gly	Cys	Arg	Gln
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Met	Gly	Phe	Leu	His	Ala	Val	Ser	Arg	Glu	Ser	Ile	Phe	Asn	Lys	Met
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Asn	Ser	Ser	Asn	Leu	Ala	Cys	Val	Phe	Gly	Leu	Asn	Leu	Ile	Trp	Pro
	370					375					380				
Ser	Gln	Gly	Val	Ser	Ser	Leu	Ser	Ala	Leu	Val	Pro	Leu	Asn	Met	Phe
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Thr	Glu	Leu	Leu	Ile	Glu	Tyr	Tyr	Glu	Lys	Ile	Phe	Ser	Thr	Pro	Glu
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Ala	Pro	Gly	Glu	His	Gly	Leu	Ala	Pro	Trp	Glu	Gln	Gly	Ser	Arg	Ala
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Ala	Pro	Leu	Gln	Glu	Ala	Val	Pro	Arg	Thr	Gln	Ala	Thr	Gly	Leu	Thr
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&lt;210&gt; 15

&lt;211&gt; 2043

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 15

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&lt;210&gt; 16

&lt;211&gt; 643

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 16

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Asp Leu Gly Lys Arg Glu Pro Ala Ala Ala Asp Glu Arg Gly Thr
20           25           30
Gln Gln Arg Arg Ala Cys Ala Asn Ala Thr Trp Asn Ser Ile His Asn
35           40           45
Gly Val Ile Ala Val Phe Gln Arg Lys Gly Leu Pro Asp Gln Glu Leu
50           55           60
Phe Ser Leu Asn Glu Gly Val Arg Gln Leu Leu Lys Thr Glu Leu Gly
65           70           75           80
Ser Phe Phe Thr Glu Tyr Leu Gln Asn Gln Leu Leu Thr Lys Gly Met
85           90           95

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Thr	Pro	Glu	Ala	Pro	Gly	Glu	His	Gly	Leu	Ala	Pro	Trp	Glu	Gln	Gly
		595					600					605			
Ser	Arg	Ala	Ala	Pro	Leu	Gln	Glu	Ala	Val	Pro	Arg	Thr	Gln	Ala	Thr
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Gly	Leu	Thr	Lys	Pro	Thr	Leu	Pro	Pro	Ser	Pro	Leu	Met	Ala	Ala	Arg
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Arg	Arg	Leu													

&lt;210&gt; 17

&lt;211&gt; 2274

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 17

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<210> 18  
 <211> 751  
 <212> PRT  
 <213> Homo sapiens

<220>  
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 <222> (1)...(751)  
 <223> Xaa = Any Amino Acid

<400> 18

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			20					25					30		
Gln	Gln	Arg	Arg	Ala	Cys	Ala	Asn	Ala	Thr	Trp	Asn	Ser	Ile	His	Asn
		35					40					45			
Gly	Val	Ile	Ala	Val	Phe	Gln	Arg	Lys	Gly	Leu	Pro	Asp	Gln	Glu	Leu
	50					55					60				
Phe	Ser	Leu	Asn	Glu	Gly	Val	Arg	Gln	Leu	Leu	Lys	Thr	Glu	Leu	Gly
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Ser	Phe	Phe	Thr	Glu	Tyr	Leu	Gln	Asn	Gln	Leu	Leu	Thr	Lys	Gly	Met
			85					90					95		
Val	Ile	Leu	Arg	Asp	Lys	Ile	Arg	Phe	Tyr	Glu	Gly	Gln	Lys	Leu	Leu
			100					105					110		
Asp	Ser	Leu	Ala	Glu	Thr	Trp	Asp	Phe	Phe	Phe	Ser	Asp	Val	Leu	Pro
		115					120					125			
Met	Leu	Gln	Ala	Ile	Phe	Tyr	Pro	Val	Gln	Gly	Lys	Glu	Pro	Ser	Val
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Arg	Gln	Leu	Ala	Leu	Leu	His	Phe	Arg	Asn	Ala	Ile	Thr	Leu	Ser	Val
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Lys	Leu	Glu	Asp	Ala	Leu	Ala	Arg	Ala	His	Ala	Arg	Val	Pro	Pro	Ala
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Ile	Val	Gln	Met	Leu	Leu	Val	Leu	Gln	Gly	Val	His	Glu	Ser	Arg	Gly
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Val	Thr	Glu	Asp	Tyr	Leu	Arg	Leu	Glu	Thr	Leu	Val	Gln	Lys	Val	Val
	195						200					205			
Ser	Pro	Tyr	Leu	Gly	Thr	Tyr	Gly	Leu	His	Ser	Ser	Glu	Gly	Pro	Phe
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		260					265						270		
Arg	His	Gly	Ile	Leu	Gln	Val	Ala	Gly	Asp	Asp	Arg	Phe	Gly	Arg	Arg
	275						280					285			
Val	Val	Thr	Phe	Ser	Cys	Cys	Arg	Met	Pro	Pro	Ser	His	Glu	Leu	Asp
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His	Gln	Arg	Leu	Leu	Glu	Tyr	Leu	Lys	Tyr	Thr	Leu	Asp	Gln	Tyr	Val
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Glu	Asn	Asp	Tyr	Thr	Ile	Val	Tyr	Phe	His	Tyr	Gly	Leu	Asn	Ser	Arg
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Asn	Lys	Pro	Ser	Leu	Gly	Trp	Leu	Gln	Ser	Ala	Tyr	Lys	Glu	Phe	Asp
		340					345					350			
Arg	Lys	Asp	Gly	Asp	Leu	Thr	Met	Trp	Pro	Arg	Leu	Val	Ser	Asn	Ser
	355						360					365			

21

Lys Leu Lys Arg Ser Ser His Leu Ser Leu Pro Lys Tyr Trp Asp Tyr  
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 Arg Tyr Lys Lys Asn Leu Lys Ala Leu Tyr Val Val His Pro Thr Ser  
 385 390 395 400  
 Phe Ile Lys Val Leu Trp Asn Ile Leu Lys Pro Leu Ile Ser His Lys  
 405 410 415  
 Phe Gly Lys Lys Val Ile Tyr Phe Asn Tyr Leu Ser Glu Leu His Glu  
 420 425 430  
 His Leu Lys Tyr Asp Gln Leu Val Ile Pro Pro Glu Val Leu Arg Tyr  
 435 440 445  
 Asp Glu Lys Leu Gln Ser Leu His Glu Gly Arg Thr Pro Pro Pro Thr  
 450 455 460  
 Lys Thr Pro Pro Pro Arg Pro Pro Leu Pro Thr Gln Gln Phe Gly Val  
 465 470 475 480  
 Ser Leu Gln Tyr Leu Lys Asp Lys Asn Gln Gly Glu Leu Ile Pro Pro  
 485 490 495  
 Val Leu Arg Phe Thr Val Thr Tyr Leu Arg Glu Lys Gly Leu Arg Thr  
 500 505 510  
 Glu Gly Leu Phe Arg Arg Ser Ala Ser Val Gln Thr Val Arg Glu Ile  
 515 520 525  
 Gln Arg Leu Tyr Asn Gln Gly Lys Pro Val Asn Phe Asp Asp Tyr Gly  
 530 535 540  
 Asp Ile His Ile Pro Ala Val Ile Leu Lys Thr Phe Leu Arg Glu Leu  
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 Pro Gln Pro Leu Leu Thr Phe Gln Ala Tyr Glu Gln Ile Leu Gly Ile  
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 Thr Cys Val Glu Ser Ser Leu Arg Val Thr Gly Cys Arg Gln Ile Leu  
 580 585 590  
 Arg Ser Leu Pro Glu His Asn Tyr Val Val Leu Arg Tyr Leu Met Gly  
 595 600 605  
 Phe Leu His Ala Val Ser Arg Glu Ser Ile Phe Asn Lys Met Asn Ser  
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 Thr Leu Pro Pro Ser Pro Leu Met Ala Ala Arg Arg Arg Leu Xaa Cys  
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&lt;210&gt; 19

&lt;211&gt; 718

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 19

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 Val Leu Arg Phe Thr Val Thr Tyr Leu Arg Glu Lys Gly Leu Arg Thr  
 500 505 510  
 Glu Gly Leu Phe Arg Arg Ser Ala Ser Val Gln Thr Val Arg Glu Ile  
 515 520 525  
 Gln Arg Leu Tyr Asn Gln Gly Lys Pro Val Asn Phe Asp Asp Tyr Gly  
 530 535 540  
 Asp Ile His Ile Pro Ala Val Ile Leu Lys Thr Phe Leu Arg Glu Leu  
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 580 585 590  
 Arg Ser Leu Pro Glu His Asn Tyr Val Val Leu Arg Tyr Leu Met Gly  
 595 600 605  
 Phe Leu His Ala Val Ser Arg Glu Ser Ile Phe Asn Lys Met Asn Ser  
 610 615 620  
 Ser Asn Leu Ala Cys Val Phe Gly Leu Asn Leu Ile Trp Pro Ser Gln  
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 Gly Val Ser Ser Leu Ser Ala Leu Val Pro Leu Asn Met Phe Thr Glu  
 645 650 655  
 Leu Leu Ile Glu Tyr Tyr Glu Lys Ile Phe Ser Thr Pro Glu Ala Pro  
 660 665 670  
 Gly Glu His Gly Leu Ala Pro Trp Glu Gln Gly Ser Arg Ala Ala Pro  
 675 680 685  
 Leu Gln Glu Ala Val Pro Arg Thr Gln Ala Thr Gly Leu Thr Lys Pro  
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&lt;210&gt; 20

&lt;211&gt; 1431

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 20

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<211> 390

<212> PRT

<213> Homo sapiens

<400> 21

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Arg	Arg	Val	Val	Thr	Phe	Ser	Cys	Cys	Arg	Met	Pro	Pro	Ser	His	Glu	35	40	45	
Leu	Asp	His	Gln	Arg	Leu	Leu	Asp	Arg	Tyr	Lys	Lys	Asn	Leu	Lys	Ala	50	55	60	
Leu	Tyr	Val	Val	His	Pro	Thr	Ser	Phe	Ile	Lys	Val	Leu	Trp	Asn	Ile	65	70	75	80
Leu	Lys	Pro	Leu	Ile	Ser	His	Lys	Phe	Gly	Lys	Lys	Val	Ile	Tyr	Phe	85	90	95	
Asn	Tyr	Leu	Ser	Glu	Leu	His	Glu	His	Leu	Lys	Tyr	Asp	Gln	Leu	Val	100	105	110	
Ile	Pro	Pro	Glu	Val	Leu	Arg	Tyr	Asp	Glu	Lys	Leu	Gln	Ser	Leu	His	115	120	125	
Glu	Gly	Arg	Thr	Pro	Pro	Pro	Thr	Lys	Thr	Pro	Pro	Pro	Arg	Pro	Pro	130	135	140	
Leu	Pro	Thr	Gln	Gln	Phe	Gly	Val	Ser	Leu	Gln	Tyr	Leu	Lys	Asp	Lys	145	150	155	160
Asn	Gln	Gly	Glu	Leu	Ile	Pro	Pro	Val	Leu	Arg	Phe	Thr	Val	Thr	Tyr	165	170	175	
Leu	Arg	Glu	Lys	Gly	Leu	Arg	Thr	Glu	Gly	Leu	Phe	Arg	Arg	Ser	Ala	180	185	190	
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Pro	Val	Asn	Phe	Asp	Asp	Tyr	Gly	Asp	Ile	His	Ile	Pro	Ala	Val	Ile	210	215	220	
Leu	Lys	Thr	Phe	Leu	Arg	Glu	Leu	Pro	Gln	Pro	Leu	Leu	Thr	Phe	Gln	225	230	235	240
Ala	Tyr	Glu	Gln	Ile	Leu	Gly	Ile	Thr	Cys	Val	Glu	Ser	Ser	Leu	Arg	245	250	255	
Val	Thr	Gly	Cys	Arg	Gln	Ile	Leu	Arg	Ser	Leu	Pro	Glu	His	Asn	Tyr	260	265	270	
Val	Val	Leu	Arg	Tyr	Leu	Met	Gly	Phe	Leu	His	Ala	Val	Ser	Arg	Glu	275	280	285	
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Leu	Asn	Leu	Ile	Trp	Pro	Ser	Gln	Gly	Val	Ser	Ser	Leu	Ser	Ala	Leu	305	310	315	320
Val	Pro	Leu	Asn	Met	Phe	Thr	Glu	Leu	Leu	Ile	Glu	Tyr	Tyr	Glu	Lys	325	330	335	
Ile	Phe	Ser	Thr	Pro	Glu	Ala	Pro	Gly	Glu	His	Gly	Leu	Ala	Pro	Trp	340	345	350	
Glu	Gln	Gly	Ser	Arg	Ala	Ala	Pro	Leu	Gln	Glu	Ala	Val	Pro	Arg	Thr	355	360	365	
Gln	Ala	Thr	Gly	Leu	Thr	Lys	Pro	Thr	Leu	Pro	Pro	Ser	Pro	Leu	Met				

25

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380

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<212> DNA  
<213> Homo sapiens

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Gly Val Ile Ala Val Phe Gln Arg Lys Gly Leu Pro Asp Gln Glu Leu  
 50 55 60  
 Phe Ser Leu Asn Glu Gly Val Arg Gln Leu Leu Lys Thr Glu Leu Gly  
 65 70 75 80  
 Ser Phe Phe Thr Glu Tyr Leu Gln Asn Gln Leu Leu Thr Lys Gly Met  
 85 90 95  
 Val Ile Leu Arg Asp Lys Ile Arg Phe Tyr Glu Gly Gln Lys Leu Leu  
 100 105 110  
 Asp Ser Leu Ala Glu Thr Trp Asp Phe Phe Phe Ser Asp Val Leu Pro  
 115 120 125  
 Met Leu Gln Ala Ile Phe Tyr Pro Val Gln Gly Lys Glu Pro Ser Val  
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 Arg Gln Leu Ala Leu Leu His Phe Arg Asn Ala Ile Thr Leu Ser Val  
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 Lys Leu Glu Asp Ala Leu Ala Arg Ala His Ala Arg Val Pro Pro Ala  
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 Val Thr Glu Asp Tyr Leu Arg Leu Glu Thr Leu Val Gln Lys Val Val  
 195 200 205  
 Ser Pro Tyr Leu Gly Thr Tyr Gly Leu His Ser Ser Glu Gly Pro Phe  
 210 215 220  
 Thr His Ser Cys Ile Leu Glu Leu Gln Arg Asp Lys Ala Ala Ala Ala  
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 260 265 270  
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 275 280 285  
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 Asn Lys Pro Ser Leu Gly Trp Leu Gln Ser Ala Tyr Lys Glu Phe Asp  
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 355 360 365  
 Lys Leu Lys Arg Ser Ser His Leu Ser Leu Pro Lys Tyr Trp Asp Tyr  
 370 375 380  
 Arg Tyr Lys Lys Asn Leu Lys Ala Leu Tyr Val Val His Pro Thr Ser  
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 Phe Ile Lys Val Leu Trp Asn Ile Leu Lys Pro Leu Ile Ser His Lys  
 405 410 415  
 Phe Gly Lys Lys Val Ile Tyr Phe Asn Tyr Leu Ser Glu Leu His Glu  
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 His Leu Lys Tyr Asp Gln Leu Val Ile Pro Pro Glu Val Leu Arg Tyr  
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 Asp Glu Lys Leu Gln Ser Leu His Glu Gly Arg Thr Pro Pro Pro Thr  
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 Lys Thr Pro Pro Pro Arg Pro Pro Leu Pro Thr Gln Gln Phe Gly Val  
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 Ser Leu Gln Tyr Leu Lys Asp Lys Asn Gln Gly Glu Leu Ile Pro Pro  
 485 490 495  
 Val Leu Arg Phe Thr Val Thr Tyr Leu Arg Glu Lys Gly Leu Pro Glu  
 500 505 510

27

His Asn Tyr Val Val Leu Arg Tyr Leu Met Gly Phe Leu His Ala Val  
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 Tyr Glu Lys Ile Phe Ser Thr Pro Glu Ala Pro Gly Glu His Gly Leu  
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<210> 25  
 <211> 379  
 <212> PRT  
 <213> Homo sapiens

<400> 25  
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Arg	Arg	Val	Val	Thr	Phe	Ser	Cys	Cys	Arg	Met	Pro	Pro	Ser	His	Glu
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Leu	Asp	His	Gln	Arg	Leu	Leu	Glu	Tyr	Leu	Lys	Tyr	Thr	Leu	Asp	Gln
		50					55					60			
Tyr	Val	Glu	Asn	Asp	Tyr	Thr	Ile	Val	Tyr	Phe	His	Tyr	Gly	Leu	Asn
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Ser	Arg	Asn	Lys	Pro	Ser	Leu	Gly	Trp	Leu	Gln	Ser	Ala	Tyr	Lys	Glu
				85					90					95	
Phe	Asp	Arg	Lys	Asp	Gly	Asp	Leu	Thr	Met	Trp	Pro	Arg	Leu	Val	Ser
			100					105					110		
Asn	Ser	Lys	Leu	Lys	Arg	Ser	Ser	His	Leu	Ser	Leu	Pro	Lys	Tyr	Trp
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Asp	Tyr	Arg	Tyr	Lys	Lys	Asn	Leu	Lys	Ala	Leu	Tyr	Val	Val	His	Pro
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Thr	Ser	Phe	Ile	Lys	Val	Leu	Trp	Asn	Ile	Leu	Lys	Pro	Leu	Ile	Ser
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His	Lys	Phe	Gly	Lys	Lys	Val	Ile	Tyr	Phe	Asn	Tyr	Leu	Ser	Glu	Leu
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His	Glu	His	Leu	Lys	Tyr	Asp	Gln	Leu	Val	Ile	Pro	Pro	Glu	Val	Leu
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Arg	Tyr	Asp	Glu	Lys	Leu	Gln	Ser	Leu	His	Glu	Gly	Arg	Thr	Pro	Pro
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Pro	Thr	Lys	Thr	Pro	Pro	Pro	Pro	Arg	Pro	Pro	Leu	Pro	Thr	Gln	Gln
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Pro	Glu	His	Asn	Tyr	Val	Val	Leu	Arg	Tyr	Leu	Met	Gly	Phe	Leu	His
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Ala	Val	Ser	Arg	Glu	Ser	Ile	Phe	Asn	Lys	Met	Asn	Ser	Ser	Asn	Leu
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Ala	Cys	Val	Phe	Gly	Leu	Asn	Leu	Ile	Trp	Pro	Ser	Gln	Gly	Val	Ser
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Ser	Leu	Ser	Ala	Leu	Val	Pro	Leu	Asn	Met	Phe	Thr	Glu	Leu	Leu	Ile
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Glu	Tyr	Tyr	Glu	Lys	Ile	Phe	Ser	Thr	Pro	Glu	Ala	Pro	Gly	Glu	His
				325					330					335	
Gly	Leu	Ala	Pro	Trp	Glu	Gln	Gly	Ser	Arg	Ala	Ala	Pro	Leu	Gln	Glu
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Ala	Val	Pro	Arg	Thr	Gln	Ala	Thr	Gly	Leu	Thr	Lys	Pro	Thr	Leu	Pro
			355				360					365			
Pro	Ser	Pro	Leu	Met	Ala	Ala	Arg	Arg	Arg	Leu					
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&lt;211&gt; 1787

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 26

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&lt;210&gt; 27

&lt;211&gt; 461

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 27

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35          40          45
Gly Val Ile Ala Val Phe Gln Arg Lys Gly Leu Pro Asp Gln Glu Leu
50          55          60
Phe Ser Leu Asn Glu Gly Val Arg Gln Leu Leu Lys Thr Glu Leu Gly
65          70          75          80
Ser Phe Phe Thr Glu Tyr Leu Gln Asn Gln Leu Leu Thr Lys Gly Met
85          90          95
Val Ile Leu Arg Asp Lys Ile Arg Phe Tyr Glu Gly Gln Lys Leu Leu
100         105         110
Asp Ser Leu Ala Glu Thr Trp Asp Phe Phe Phe Ser Asp Val Leu Pro
115         120         125
Met Leu Gln Ala Ile Phe Tyr Pro Val Gln Gly Lys Glu Pro Ser Val
130         135         140
Arg Gln Leu Ala Leu Leu His Phe Arg Asn Ala Ile Thr Leu Ser Val
145         150         155         160
Lys Leu Glu Asp Ala Leu Ala Arg Ala His Ala Arg Val Pro Pro Ala
165         170         175
Ile Val Gln Met Leu Leu Val Leu Gln Gly Val His Glu Ser Arg Gly
180         185         190
Val Thr Glu Asp Tyr Leu Arg Leu Glu Thr Leu Val Gln Lys Val Val
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 245 250 255  
 Gly Gln Asp Pro Ala Leu Ser Thr Ser His Pro Phe Tyr Asp Val Ala  
 260 265 270  
 Arg His Gly Ile Leu Gln Val Ala Gly Asp Asp Arg Phe Gly Arg Arg  
 275 280 285  
 Val Val Thr Phe Ser Cys Cys Arg Met Pro Pro Ser His Glu Leu Asp  
 290 295 300  
 His Gln Arg Leu Leu Glu Tyr Lys Lys Asn Leu Lys Ala Leu Tyr Val  
 305 310 315 320  
 Val His Pro Thr Ser Phe Ile Lys Val Leu Trp Asn Ile Leu Lys Pro  
 325 330 335  
 Leu Ile Ser His Lys Phe Gly Lys Lys Val Ile Tyr Phe Asn Tyr Leu  
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 Ser Glu Leu His Glu His Leu Lys Tyr Asp Gln Leu Val Ile Pro Pro  
 355 360 365  
 Glu Val Leu Arg Tyr Asp Glu Lys Leu Gln Ser Leu His Glu Gly Arg  
 370 375 380  
 Thr Pro Pro Pro Thr Lys Thr Pro Pro Pro Arg Pro Pro Leu Pro Thr  
 385 390 395 400  
 Gln Gln Phe Gly Val Ser Leu Gln Tyr Leu Lys Asp Lys Asn Gln Gly  
 405 410 415  
 Glu Leu Ile Pro Pro Val Leu Arg Phe Thr Val Thr Tyr Leu Arg Glu  
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 <212> DNA  
 <213> Homo sapiens

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&lt;211&gt; 975

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 31

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Lys Gln Gln Tyr Asp Glu Leu Glu Ala Glu Tyr Asp Ser Leu Lys Gln
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      100          105          110
Gln Asn Glu Leu Lys Gln Ser Arg Ala Val Val Thr Asn Val Gln Ala
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      130          135          140
Glu Met Val Glu Leu Gln Arg Ile Arg Met Lys Asp Glu Ile Arg Glu
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Tyr Lys Phe Arg Glu Ala Arg Leu Leu Gln Asp Tyr Thr Glu Leu Glu
      165          170          175
Glu Glu Asn Ile Thr Leu Gln Lys Leu Val Ser Thr Leu Lys Gln Asn
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      305          310          315          320
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      325          330          335
Glu Arg Glu Lys Ala Ile Leu Leu Ala Asn Leu Gln Glu Ser Gln Thr
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Gln Leu Glu His Thr Lys Gly Ala Leu Thr Glu Gln His Glu Arg Val
      355          360          365
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      370          375          380
Lys Glu Leu Lys Ala Glu Leu Asp Gly Glu Lys Gly Arg Asp Ser Gly
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Glu Glu Ala His Asp Tyr Glu Val Asp Ile Asn Gly Leu Glu Ile Leu
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Thr Pro Asn Arg Val Met Leu Asp Tyr Tyr Arg Gln Ser Arg Val Thr		
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Ser Pro Thr Lys Thr Pro Thr Ile Ser Pro Val Ile Thr Ala Pro Pro		
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Ile Tyr Asn Leu Asn Ala Ile Ile Arg Asp Gln Ile Lys His Leu Gln		
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Lys Ala Val Asp Arg Ser Leu Gln Leu Ser Arg Gln Arg Ala Ala Ala		
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Arg Glu Leu Ala Pro Met Ile Asp Lys Asp Lys Glu Ala Leu Met Glu		
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Glu Ile Leu Lys Leu Lys Ser Leu Leu Ser Thr Lys Arg Glu Gln Ile		
675	680	685
Ala Thr Leu Arg Ala Val Leu Lys Ala Asn Lys Gln Thr Ala Glu Val		
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Ala Leu Ala Asn Leu Lys Asn Lys Tyr Glu Asn Glu Lys Ala Met Val		
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Thr Glu Thr Met Thr Lys Leu Arg Asn Glu Leu Lys Ala Leu Lys Glu		
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Asp Ala Ala Thr Phe Ser Ser Leu Arg Thr Met Phe Ala Thr Arg Cys		
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Asp Glu Tyr Val Thr Gln Leu Asp Glu Met Gln Arg Gln Leu Ala Ala		
755	760	765
Ala Glu Asp Glu Lys Lys Thr Leu Asn Thr Leu Leu Arg Met Ala Ile		
770	775	780
Gln Gln Lys Leu Ala Leu Thr Gln Arg Leu Glu Asp Leu Glu Phe Asp		
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His Glu Gln Ser Arg Arg Ser Lys Gly Lys Leu Gly Lys Ser Lys Ile		
805	810	815
Gly Ser Pro Lys Val Ser Gly Glu Ala Ser Val Thr Val Pro Thr Ile		
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Asp Thr Tyr Leu Leu His Ser Gln Gly Pro Gln Thr Pro Asn Ile Arg		
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Leu Arg Val Pro Pro Asp Pro Thr Ser Thr Glu Ser Phe Leu Leu Lys		
885	890	895
Gly Pro Pro Ser Met Ser Glu Phe Ile Gln Gly His Arg Leu Ser Lys		

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Ser Val Pro Pro Gln Cys Ser Gln Leu Ala Gly Arg Gln Asp Cys Pro					
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 <213> Homo sapiens

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          35          40          45
His Tyr Lys His His Trp Phe Pro Glu Lys Pro Ser Lys Gly Ser Gly
          50          55          60
Tyr Arg Cys Ile Arg Ile Asn His Lys Met Asp Pro Ile Ile Ser Arg
          65          70          75          80
Val Ala Ser Gln Ile Gly Leu Ser Gln Pro Gln Leu His Gln Leu Leu
          85          90          95
Pro Ser Glu Leu Thr Leu Trp Val Asp Pro Tyr Glu Val Ser Tyr Arg
          100          105          110
Ile Gly Glu Asp Gly Ser Ile Cys Val Leu Tyr Glu Glu Ala Pro Leu
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&lt;210&gt; 35

&lt;211&gt; 1390

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 35

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Ala Pro Pro Thr Phe Cys Thr Pro Ser Arg Gly Leu Gln Arg Pro Arg
20      25      30
Ser Pro Gly Ala Thr Met Leu Asp Pro Ser Ser Ser Glu Glu Glu Ser
35      40      45
Asp Glu Ile Val Glu Glu Glu Ser Gly Lys Glu Val Leu Gly Ser Ala
50      55      60
Pro Ser Gly Ala Arg Leu Ser Pro Ser Arg Thr Ser Glu Gly Ser Ala
65      70      75      80
Gly Ser Ala Gly Leu Gly Gly Gly Gly Ala Gly Ala Gly Ala Gly Val
85      90      95
Gly Ala Gly Gly Gly Gly Gly Ser Gly Ala Ser Ser Gly Gly Gly Ala
100     105     110
Gly Gly Leu Gln Pro Ser Ser Arg Ala Gly Gly Gly Arg Pro Ser Ser
115     120     125
Pro Ser Pro Ser Val Val Ser Glu Lys Glu Lys Glu Glu Leu Glu Arg
130     135     140
Leu Gln Lys Glu Glu Glu Glu Arg Lys Lys Arg Leu Gln Leu Tyr Val
145     150     155     160
Phe Val Met Arg Cys Ile Ala Tyr Pro Phe Asn Ala Lys Gln Pro Thr
165     170     175
Asp Met Ala Arg Arg Gln Gln Lys Ile Ser Lys Gln Gln Leu Gln Thr
180     185     190
Val Lys Asp Arg Phe Gln Ala Phe Leu Asn Gly Glu Thr Gln Ile Met
195     200     205
Ala Asp Glu Ala Phe Met Asn Ala Val Gln Ser Tyr Tyr Glu Val Phe
210     215     220
Leu Lys Ser Asp Arg Val Ala Arg Met Val Gln Ser Gly Gly Cys Ser
225     230     235     240
Ala Asn Asp Ser Arg Glu Val Phe Lys Lys His Ile Glu Lys Arg Val
245     250     255
Arg Ser Leu Pro Glu Ile Asp Gly Leu Ser Lys Glu Thr Val Leu Ser
260     265     270
Ser Trp Met Ala Lys Phe Asp Ala Ile Tyr Arg Gly Glu Glu Asp Pro

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275	280	285
Arg Lys Gln Gln Ala	Arg Met Thr Ala Ser Ala	Ala Ser Glu Leu Ile
290	295	300
Leu Ser Lys Glu Gln	Leu Tyr Glu Met Phe	Gln Asn Ile Leu Gly Ile
305	310	315
Lys Lys Phe Glu His	Gln Leu Leu Tyr Asn	Ala Cys Gln Leu Asp Asn
325	330	335
Pro Asp Glu Gln Ala	Ala Gln Ile Arg Arg	Glu Leu Asp Gly Arg Leu
340	345	350
Gln Met Ala Asp Gln	Ile Ala Arg Glu Arg	Lys Phe Pro Lys Phe Val
355	360	365
Ser Lys Glu Met Glu	Asn Met Tyr Ile Glu	Glu Leu Lys Ser Ser Val
370	375	380
Asn Leu Leu Met Ala	Asn Leu Glu Ser Met	Pro Val Ser Lys Gly Gly
385	390	395
Glu Phe Lys Leu Gln	Lys Leu Lys Arg Ser	His Asn Ala Ser Ile Ile
405	410	415
Asp Met Gly Glu Glu	Ser Glu Asn Gln Leu	Ser Lys Ser Asp Val Val
420	425	430
Leu Ser Phe Ser Leu	Glu Val Val Ile Met	Glu Val Gln Gly Leu Lys
435	440	445
Ser Leu Ala Pro Asn	Arg Ile Val Tyr Cys	Thr Met Glu Val Glu Gly
450	455	460
Gly Glu Lys Leu Gln	Thr Asp Gln Ala Glu	Ala Ser Lys Pro Thr Trp
465	470	475
Gly Thr Gln Gly Asp	Phe Ser Thr Thr His	Ala Leu Pro Ala Val Lys
485	490	495
Val Lys Leu Phe Thr	Glu Ser Thr Gly Val	Leu Ala Leu Glu Asp Lys
500	505	510
Glu Leu Gly Arg Val	Ile Leu His Pro Thr	Pro Asn Ser Pro Lys Gln
515	520	525
Ser Glu Trp His Lys	Met Thr Val Ser Lys	Asn Cys Pro Asp Gln Asp
530	535	540
Leu Lys Ile Lys Leu	Ala Val Arg Met Asp	Lys Pro Gln Asn Met Lys
545	550	555
His Ser Gly Tyr Leu	Trp Ala Ile Gly Lys	Asn Val Trp Lys Arg Trp
565	570	575
Lys Lys Arg Phe Phe	Val Leu Val Gln Val	Ser Gln Tyr Thr Phe Ala
580	585	590
Met Cys Ser Tyr Arg	Glu Lys Lys Ala Glu	Pro Gln Glu Leu Leu Gln
595	600	605
Leu Asp Gly Tyr Thr	Val Asp Tyr Thr Asp	Pro Gln Pro Gly Leu Glu
610	615	620
Gly Gly Arg Ala Phe	Phe Asn Ala Val Lys	Glu Gly Asp Thr Val Ile
625	630	635
Phe Ala Ser Asp Asp	Glu Gln Asp Arg Ile	Leu Trp Val Gln Ala Met
645	650	655
Tyr Arg Ala Thr Gly	Gln Ser His Lys Pro	Val Pro Pro Thr Gln Val
660	665	670
Gln Lys Leu Asn Ala	Lys Gly Gly Asn Val	Pro Gln Leu Asp Ala Pro
675	680	685
Ile Ser Gln Phe Tyr	Ala Asp Arg Ala Gln	Lys His Gly Met Asp Glu
690	695	700
Phe Ile Ser Ser Asn	Pro Cys Asn Phe Asp	His Ala Ser Leu Phe Glu
705	710	715
Met Val Gln Arg Leu	Thr Leu Asp His Arg	Leu Asn Asp Ser Tyr Ser
725	730	735
Cys Leu Gly Trp Phe	Ser Pro Gly Gln Val	Phe Val Leu Asp Glu Tyr

[illegible]

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1220	1225	1230
Leu Ser Arg Tyr Asp Glu Gly Thr Leu Phe Ser Ser Phe Leu Ser Phe		
1235	1240	1245
Thr Val Lys Ala Ala Ser Lys Tyr Val Asp Val Pro Lys Pro Gly Met		
1250	1255	1260
Asp Val Ala Asp Ala Tyr Val Thr Phe Val Arg His Ser Gln Asp Val		
1265	1270	1275
Leu Arg Asp Lys Val Asn Glu Glu Met Tyr Ile Glu Arg Leu Phe Asp		
1285	1290	1295
Gln Trp Tyr Asn Ser Ser Met Asn Val Ile Cys Thr Trp Leu Thr Asp		
1300	1305	1310
Arg Met Asp Leu Gln Leu His Ile Tyr Gln Leu Lys Thr Leu Ile Arg		
1315	1320	1325
Val Val Lys Lys Thr Tyr Arg Asp Phe Arg Leu Gln Gly Val Leu Asp		
1330	1335	1340
Ser Thr Leu Asn Ser Lys Thr Tyr Glu Thr Ile Arg Asn Arg Leu Thr		
1345	1350	1355
Val Glu Glu Ala Thr Ala Ser Val Ser Glu Gly Gly Gly Leu Gln Gly		
1365	1370	1375
Ile Ser Met Lys Asp Ser Asp Glu Glu Asp Glu Glu Asp Asp		
1380	1385	1390

&lt;210&gt; 36

&lt;211&gt; 4828

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 36

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&lt;210&gt; 37

&lt;211&gt; 882

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 37

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 20          25          30
Asp Ala Glu Ser Tyr Thr Phe Thr Val Pro Arg Arg His Leu Glu Arg
 35          40          45
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 50          55          60
Arg Thr Ala Tyr Phe Ser Leu Asp Thr Arg Phe Lys Val Gly Thr Asp
 65          70          75          80
Gly Val Ile Thr Val Lys Arg Pro Leu Arg Phe His Asn Pro Gln Ile
 85          90          95
His Phe Leu Val Tyr Ala Trp Asp Ser Thr Tyr Arg Lys Phe Ser Thr
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Lys Val Thr Leu Asn Thr Val Gly His His His Arg Pro Pro His
 115         120         125
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 130         135         140
Ser Ser Pro Gly Leu Arg Arg Gln Lys Arg Asp Trp Val Ile Pro Pro
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Ile Ser Cys Pro Glu Asn Glu Lys Gly Pro Phe Pro Lys Asn Leu Val
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Gln Ile Lys Ser Asn Lys Asp Lys Glu Gly Lys Val Phe Tyr Ser Ile
 180         185         190
Thr Gly Gln Gly Ala Asp Thr Pro Pro Val Gly Val Phe Ile Ile Glu
 195         200         205
Arg Glu Thr Gly Trp Leu Lys Val Thr Glu Pro Leu Asp Arg Glu Arg
 210         215         220
Ile Ala Thr Tyr Thr Leu Phe Ser His Ala Val Ser Ser Asn Gly Asn
 225         230         235         240
Ala Val Glu Asp Pro Met Glu Ile Leu Ile Thr Val Thr Asp Gln Asn
 245         250         255
Asp Asn Lys Pro Glu Phe Thr Gln Glu Val Phe Lys Gly Ser Val Met
 260         265         270
Glu Gly Ala Leu Pro Gly Thr Ser Val Met Glu Val Thr Ala Thr Asp
 275         280         285
Ala Asp Asp Asp Val Asn Thr Tyr Asn Ala Ala Ile Ala Tyr Thr Ile
 290         295         300
Leu Ser Gln Asp Pro Glu Leu Pro Asp Lys Asn Met Phe Thr Ile Asn
 305         310         315         320
Arg Asn Thr Gly Val Ile Ser Val Val Thr Thr Gly Leu Asp Arg Glu
 325         330         335
Ser Phe Pro Thr Tyr Thr Leu Val Val Gln Ala Ala Asp Leu Gln Gly
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Glu Gly Leu Ser Thr Thr Ala Thr Ala Val Ile Thr Val Thr Asp Thr
 355         360         365
Asn Asp Asn Pro Pro Ile Phe Asn Pro Thr Thr Tyr Lys Gly Gln Val
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Asp Gly Ile Leu Lys Thr Ala Lys Gly Leu Asp Phe Glu Ala Lys Gln

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595	600	605
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785	790	795
Pro Ala Asn Pro Asp Glu	Ile Gly Asn Phe Ile Asp	Glu Asn Leu Lys
805	810	815
Ala Ala Asp Thr Asp Pro	Thr Ala Pro Pro Tyr Asp	Ser Leu Leu Val
820	825	830
Phe Asp Tyr Glu Gly Ser	Gly Ser Glu Ala Ala Ser	Leu Ser Ser Leu
835	840	845
Asn Ser Ser Glu Ser Asp	Lys Asp Gln Asp Tyr Asp	Tyr Leu Asn Glu
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Trp Gly Asn Arg Phe Lys	Lys Leu Ala Asp Met Tyr	Gly Gly Gly Glu
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Asp Asp		880

<210> 38  
 <211> 4521  
 <212> DNA  
 <213> Homo sapiens

<400> 38

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&lt;210&gt; 39

&lt;211&gt; 790

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 39

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20          25          30
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35          40          45
Asn Arg Ser Lys Arg Ser Trp Met Trp Asn Gln Phe Phe Leu Leu Glu
50          55          60
Glu Tyr Thr Gly Ser Asp Tyr Gln Tyr Val Gly Lys Leu His Ser Asp
65          70          75          80
Gln Asp Arg Gly Asp Gly Ser Leu Lys Tyr Ile Leu Ser Gly Asp Gly
85          90          95
Ala Gly Asp Leu Phe Ile Ile Asn Glu Asn Thr Gly Asp Ile Gln Ala
100         105         110
Thr Lys Arg Leu Asp Arg Glu Glu Lys Pro Val Tyr Ile Leu Arg Ala
115         120         125
Gln Ala Ile Asn Arg Arg Thr Gly Arg Pro Val Glu Pro Glu Ser Glu
130         135         140
Phe Ile Ile Lys Ile His Asp Ile Asn Asp Asn Glu Pro Ile Phe Thr
145         150         155         160
Lys Glu Val Tyr Thr Ala Thr Val Pro Glu Met Ser Asp Val Gly Thr
165         170         175
Phe Val Val Gln Val Thr Ala Thr Asp Ala Asp Asp Pro Thr Tyr Gly
180         185         190
Asn Ser Ala Lys Val Val Tyr Ser Ile Leu Gln Gly Gln Pro Tyr Phe
195         200         205

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Met	Gly	Gly	Gln	Met	Gly	Gly	Leu	Ser	Gly	Thr	Thr	Thr	Val	Asn	Ile
				245					250					255	
Thr	Leu	Thr	Asp	Val	Asn	Asp	Asn	Pro	Pro	Arg	Phe	Pro	Gln	Ser	Thr
			260					265					270		
Tyr	Gln	Phe	Lys	Thr	Pro	Glu	Ser	Ser	Pro	Pro	Gly	Thr	Pro	Ile	Gly
		275						280				285			
Arg	Ile	Lys	Ala	Ser	Asp	Ala	Asp	Val	Gly	Glu	Asn	Ala	Glu	Ile	Glu
290						295					300				
Tyr	Ser	Ile	Thr	Asp	Gly	Glu	Gly	Leu	Asp	Met	Phe	Asp	Val	Ile	Thr
305					310					315					320
Asp	Gln	Glu	Thr	Gln	Glu	Gly	Ile	Ile	Thr	Val	Lys	Lys	Leu	Leu	Asp
				325					330					335	
Phe	Glu	Lys	Lys	Lys	Val	Tyr	Thr	Leu	Lys	Val	Glu	Ala	Ser	Asn	Pro
			340					345					350		
Tyr	Val	Glu	Pro	Arg	Phe	Leu	Tyr	Leu	Gly	Pro	Phe	Lys	Asp	Ser	Ala
		355					360				365				
Thr	Val	Arg	Ile	Val	Val	Glu	Asp	Val	Asp	Glu	Pro	Pro	Val	Phe	Ser
370						375					380				
Lys	Leu	Ala	Tyr	Ile	Leu	Gln	Ile	Arg	Glu	Asp	Ala	Gln	Ile	Asn	Thr
385					390					395					400
Thr	Ile	Gly	Ser	Val	Thr	Ala	Gln	Asp	Pro	Asp	Ala	Ala	Arg	Asn	Pro
				405					410					415	
Val	Lys	Tyr	Ser	Val	Asp	Arg	His	Thr	Asp	Met	Asp	Arg	Ile	Phe	Asn
			420					425					430		
Ile	Asp	Ser	Gly	Asn	Gly	Ser	Ile	Phe	Thr	Ser	Lys	Leu	Leu	Asp	Arg
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Glu	Thr	Leu	Leu	Trp	His	Asn	Ile	Thr	Val	Ile	Ala	Thr	Glu	Ile	Asn
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Asn	Pro	Lys	Gln	Ser	Ser	Arg	Val	Pro	Leu	Tyr	Ile	Lys	Val	Leu	Asp
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Val	Asn	Asp	Asn	Ala	Pro	Glu	Phe	Ala	Glu	Phe	Tyr	Glu	Thr	Phe	Val
				485					490					495	
Cys	Glu	Lys	Ala	Lys	Ala	Asp	Gln	Leu	Ile	Gln	Thr	Leu	His	Ala	Val
			500					505					510		
Asp	Lys	Asp	Asp	Pro	Tyr	Ser	Gly	His	Gln	Phe	Ser	Phe	Ser	Leu	Ala
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Pro	Glu	Ala	Ala	Ser	Gly	Ser	Asn	Phe	Thr	Ile	Gln	Asp	Asn	Lys	Asp
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Asn	Thr	Ala	Gly	Ile	Leu	Thr	Arg	Lys	Asn	Gly	Tyr	Asn	Arg	His	Glu
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Met	Ser	Thr	Tyr	Leu	Leu	Pro	Val	Val	Ile	Ser	Asp	Asn	Asp	Tyr	Pro
				565					570					575	
Val	Gln	Ser	Ser	Thr	Gly	Thr	Val	Thr	Val	Arg	Val	Cys	Ala	Cys	Asp
			580					585					590		
His	His	Gly	Asn	Met	Gln	Ser	Cys	His	Ala	Glu	Ala	Leu	Ile	His	Pro
		595					600					605			
Thr	Gly	Leu	Ser	Thr	Gly	Ala	Leu	Val	Ala	Ile	Leu	Leu	Cys	Ile	Val
		610				615					620				
Ile	Leu	Leu	Val	Thr	Val	Val	Leu	Phe	Ala	Ala	Leu	Arg	Arg	Gln	Arg
625					630					635					640
Lys	Lys	Glu	Pro	Leu	Ile	Ile	Ser	Lys	Glu	Asp	Ile	Arg	Asp	Asn	Ile
				645					650					655	
Val	Ser	Tyr	Asn	Asp	Glu	Gly	Gly	Gly	Glu	Glu	Asp	Thr	Gln	Ala	Phe
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Asp Ile Gly Thr Leu Arg Asn Pro Glu Ala Ile Glu Asp Asn Lys Leu  
 675 680 685  
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 690 695 700  
 Thr Ala Arg Asp Asn Thr Asp Val Arg Asp Phe Ile Asn Gln Arg Leu  
 705 710 715 720  
 Lys Glu Asn Asp Thr Asp Pro Thr Ala Pro Pro Tyr Asp Ser Leu Ala  
 725 730 735  
 Thr Tyr Ala Tyr Glu Gly Thr Gly Ser Val Ala Asp Ser Leu Ser Ser  
 740 745 750  
 Leu Glu Ser Val Thr Thr Asp Ala Asp Gln Asp Tyr Asp Tyr Leu Ser  
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 <211> 987  
 <212> DNA  
 <213> Homo sapiens

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 <211> 156  
 <212> PRT  
 <213> Homo sapiens

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 35 40 45  
 Ile Gln Val Met Met Met Gly Ser Ala Arg Val Ala Glu Leu Leu Leu  
 50 55 60  
 Leu His Gly Ala Glu Pro Asn Cys Ala Asp Pro Ala Thr Leu Thr Arg  
 65 70 75 80

Pro	Val	His	Asp	Ala	Ala	Arg	Glu	Gly	Phe	Leu	Asp	Thr	Leu	Val	Val
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Leu	His	Arg	Ala	Gly	Ala	Arg	Leu	Asp	Val	Arg	Asp	Ala	Trp	Gly	Arg
			100					105					110		
Leu	Pro	Val	Asp	Leu	Ala	Glu	Glu	Leu	Gly	His	Arg	Asp	Val	Ala	Arg
			115				120					125			
Tyr	Leu	Arg	Ala	Ala	Ala	Gly	Gly	Thr	Arg	Gly	Ser	Asn	His	Ala	Arg
			130				135					140			
Ile	Asp	Ala	Ala	Glu	Gly	Pro	Ser	Asp	Ile	Pro	Asp				
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&lt;210&gt; 42

&lt;211&gt; 5142

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 42

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&lt;210&gt; 43

&lt;211&gt; 1203

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 43

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Gly Val Gln Ile Arg Phe Ile Thr Glu Pro Val Ser Gly Ala Glu Met
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Gly Thr Leu Arg Arg Gly Gly Arg Arg Pro Ala Lys Asp Ala Arg Ala

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Leu	Arg	Arg	Ser	Met	Gln	Asp	Ala	Thr	Gln	Asp	His	Ala	Val	Leu	Glu
	530					535					540				
Ala	Glu	Arg	Gln	Lys	Met	Ser	Ala	Leu	Val	Arg	Gly	Leu	Gln	Arg	Glu
	545					550					555				560
Leu	Glu	Glu	Thr	Ser	Glu	Glu	Thr	Gly	His	Trp	Gln	Ser	Met	Phe	Gln
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Lys	Asn	Lys	Glu	Asp	Leu	Arg	Ala	Thr	Lys	Gln	Glu	Leu	Leu	Gln	Leu
			580						585					590	
Arg	Met	Glu	Lys	Glu	Met	Glu	Glu	Leu	Gly	Glu	Lys	Ile	Glu		
		595				600					605				
Val	Leu	Gln	Arg	Glu	Leu	Glu	Gln	Ala	Arg	Ala	Ser	Ala	Gly	Asp	Thr
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Arg	Gln	Val	Glu	Val	Leu	Lys	Lys	Glu	Leu	Leu	Arg	Thr	Gln	Glu	Glu
	625					630					635				640
Leu	Lys	Glu	Leu	Gln	Ala	Glu	Arg	Gln	Ser	Gln	Glu	Val	Ala	Gly	Arg
			645						650					655	
His	Arg	Asp	Arg	Glu	Leu	Glu	Lys	Gln	Leu	Ala	Val	Leu	Arg	Val	Glu
			660					665					670		
Ala	Asp	Arg	Gly	Arg	Glu	Leu	Glu	Glu	Gln	Asn	Leu	Gln	Leu	Gln	Lys
		675					680					685			
Thr	Leu	Gln	Gln	Leu	Arg	Gln	Asp	Cys	Glu	Glu	Ala	Ser	Lys	Ala	Lys
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Val	Glu	Thr	Thr	Leu	Arg	Glu	Thr	Gln	Glu	Glu	Asn	Asp	Glu	Phe	Arg
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Arg	Arg	Ile	Leu	Gly	Leu	Glu	Gln	Gln	Leu	Lys	Glu	Thr	Arg	Gly	Leu
		740					745						750		
Val	Asp	Gly	Gly	Glu	Ala	Val	Glu	Ala	Arg	Leu	Arg	Asp	Lys	Leu	Gln
		755					760					765			
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Gln	Glu	Glu	Glu	Gly	Ser	Leu	Ala	Ala	Ala	Lys	Arg	Ala	Leu	Glu	Ala
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Arg	Leu	Glu	Glu	Ala	Gln	Arg	Gly	Leu	Ala	Arg	Leu	Gly	Gln	Glu	Gln
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Ser	Lys	Gln	Ala	Leu	Gln	Gln	Leu	Gln	Ala	Gln	Leu	Glu	Asp	Tyr	Lys
	865					870					875				880
Glu	Lys	Ala	Arg	Arg	Glu	Val	Ala	Asp	Ala	Gln	Arg	Gln	Ala	Lys	Asp
			885					890						895	
Trp	Ala	Ser	Glu	Ala	Glu	Lys	Thr	Ser	Gly	Gly	Leu	Ser	Arg	Leu	Gln
		900					905						910		
Asp	Glu	Ile	Gln	Arg	Leu	Arg	Gln	Ala	Leu	Gln	Ala	Ser	Gln	Ala	Glu
		915					920					925			
Arg	Asp	Thr	Ala	Arg	Leu	Asp	Lys	Glu	Leu	Leu	Ala	Gln	Arg	Leu	Gln
	930					935					940				
Gly	Leu	Glu	Gln	Glu	Ala	Glu	Asn	Lys	Lys	Arg	Ser	Gln	Asp	Asp	Arg
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Ala	Arg	Gln	Leu	Lys	Gly	Leu	Glu	Glu	Lys	Val	Ser	Arg	Leu	Glu	Thr

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<210> 44
<211> 1925
<212> DNA
<213> Homo sapiens
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atgtt 1925

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&lt;210&gt; 45

&lt;211&gt; 383

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 45

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          20          25          30
Gln Tyr Arg Glu Gly Asp Gly Ser Cys Phe Pro Asp Ala Leu Asp Arg
          35          40          45
Phe Leu Cys Thr His Ile Ile Tyr Ser Phe Ala Asn Ile Ser Asn Asp
          50          55          60
His Ile Asp Thr Trp Glu Trp Asn Asp Val Thr Leu Tyr Gly Met Leu
          65          70          75          80
Asn Thr Leu Lys Asn Arg Asn Pro Asn Leu Lys Thr Leu Leu Ser Val
          85          90          95
Gly Gly Trp Asn Phe Gly Ser Gln Arg Phe Ser Lys Ile Ala Ser Asn
          100          105          110
Thr Gln Ser Arg Arg Thr Phe Ile Lys Ser Val Pro Pro Phe Leu Arg
          115          120          125
Thr His Gly Phe Asp Gly Leu Asp Leu Ala Trp Leu Tyr Pro Gly Arg
          130          135          140
Arg Asp Lys Gln His Phe Thr Thr Leu Ile Lys Glu Met Lys Ala Glu
          145          150          155          160
Phe Ile Lys Glu Ala Gln Pro Gly Lys Lys Gln Leu Leu Leu Ser Ala
          165          170          175
Ala Leu Ser Ala Gly Lys Val Thr Ile Asp Ser Ser Tyr Asp Ile Ala
          180          185          190
Lys Ile Ser Gln His Leu Asp Phe Ile Ser Ile Met Thr Tyr Asp Phe
          195          200          205
His Gly Ala Trp Arg Gly Thr Thr Gly His His Ser Pro Leu Phe Arg
          210          215          220
Gly Gln Glu Asp Ala Ser Pro Asp Arg Phe Ser Asn Thr Asp Tyr Ala
          225          230          235          240
Val Gly Tyr Met Leu Arg Leu Gly Ala Pro Ala Ser Lys Leu Val Met
          245          250          255
Gly Ile Pro Thr Phe Gly Arg Ser Phe Thr Leu Ala Ser Ser Glu Thr
          260          265          270
Gly Val Gly Ala Pro Ile Ser Gly Pro Gly Ile Pro Gly Arg Phe Thr
          275          280          285
Lys Glu Ala Gly Thr Leu Ala Tyr Tyr Glu Ile Cys Asp Phe Leu Arg

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55

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Lys Val Gln Tyr Leu Lys Asp Arg Gln Leu Ala Gly Ala Met Val Trp		
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Ala Leu Asp Leu Asp Asp Phe Gln Gly Ser Phe Cys Gly Gln Asp Leu		
	355	360
Arg Phe Pro Leu Thr Asn Ala Ile Lys Asp Ala Leu Ala Ala Thr		
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<210> 46  
 <211> 1528  
 <212> DNA  
 <213> Homo sapiens

<400> 46  
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<210> 47  
 <211> 417  
 <212> PRT  
 <213> Homo sapiens

<400> 47  
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 Arg Pro Glu Pro Val Arg Ala Ala Ser Glu Arg Arg Arg Leu Tyr Pro  
 35 40 45

Pro Ser Ala Glu Tyr Pro Asp Leu Arg Lys His Asn Asn Cys Met Ala  
 50 55 60  
 Ser His Leu Thr Pro Ala Val Tyr Ala Arg Leu Cys Asp Lys Thr Thr  
 65 70 75 80  
 Pro Thr Gly Trp Thr Leu Asp Gln Cys Ile Gln Thr Gly Val Asp Asn  
 85 90 95  
 Pro Gly His Pro Phe Ile Lys Thr Val Gly Met Val Ala Gly Asp Glu  
 100 105 110  
 Glu Thr Tyr Glu Val Phe Ala Asp Leu Phe Asp Pro Val Ile Gln Glu  
 115 120 125  
 Arg His Asn Gly Tyr Asp Pro Arg Thr Met Lys His Thr Thr Asp Leu  
 130 135 140  
 Asp Ala Ser Lys Ile Arg Ser Gly Tyr Phe Asp Glu Arg Tyr Val Leu  
 145 150 155 160  
 Ser Ser Arg Val Arg Thr Gly Arg Ser Ile Arg Gly Leu Ser Leu Pro  
 165 170 175  
 Pro Ala Cys Thr Arg Ala Glu Arg Arg Glu Val Glu Arg Val Val Val  
 180 185 190  
 Asp Ala Leu Ser Gly Leu Lys Gly Asp Leu Ala Gly Arg Tyr Tyr Arg  
 195 200 205  
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 Phe Leu Phe Asp Lys Pro Val Ser Pro Leu Leu Thr Ala Ala Gly Met  
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 245 250 255  
 Ser Phe Leu Ile Trp Val Asn Glu Glu Asp His Thr Arg Val Ile Ser  
 260 265 270  
 Met Glu Lys Gly Gly Asn Met Lys Arg Val Phe Glu Arg Phe Cys Arg  
 275 280 285  
 Gly Leu Lys Glu Val Glu Arg Leu Ile Gln Glu Arg Gly Trp Glu Phe  
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 Met Trp Asn Glu Arg Leu Gly Tyr Ile Leu Thr Cys Pro Ser Asn Leu  
 305 310 315 320  
 Gly Thr Gly Leu Arg Ala Gly Val His Ile Lys Leu Pro Leu Leu Ser  
 325 330 335  
 Lys Asp Ser Arg Phe Pro Lys Ile Leu Glu Asn Leu Arg Leu Gln Lys  
 340 345 350  
 Arg Gly Thr Gly Gly Val Asp Thr Ala Ala Thr Gly Gly Val Phe Asp  
 355 360 365  
 Ile Ser Asn Leu Asp Arg Leu Gly Lys Ser Glu Val Glu Leu Val Gln  
 370 375 380  
 Leu Val Ile Asp Gly Val Asn Tyr Leu Ile Asp Cys Glu Arg Arg Leu  
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 405 410 415  
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&lt;210&gt; 48

&lt;211&gt; 2365

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 48

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&lt;210&gt; 49

&lt;211&gt; 228

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 49

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Met Ala Ser Thr Ala Ser Glu Ile Ile Ala Phe Met Val Ser Ile Ser
 1             5             10            15
Gly Trp Val Leu Val Ser Ser Thr Leu Pro Thr Asp Tyr Trp Lys Val
 20            25            30
Ser Thr Ile Asp Gly Thr Val Ile Thr Thr Ala Thr Tyr Trp Ala Asn
 35            40            45
Leu Trp Lys Ala Cys Val Thr Asp Ser Thr Gly Val Ser Asn Cys Lys
 50            55            60
Asp Phe Pro Ser Met Leu Ala Leu Asp Gly Tyr Ile Gln Ala Cys Arg
 65            70            75            80
Gly Leu Met Ile Ala Ala Val Ser Leu Gly Phe Phe Gly Ser Ile Phe
 85            90            95
Ala Leu Phe Gly Met Lys Cys Thr Lys Val Gly Gly Ser Asp Lys Ala

```

```

      100      105      110
Lys Ala Lys Ile Ala Cys Leu Ala Gly Ile Val Phe Ile Leu Ser Gly
      115      120      125
Leu Cys Ser Met Thr Gly Cys Ser Leu Tyr Ala Asn Lys Ile Thr Thr
      130      135      140
Glu Phe Phe Asp Pro Leu Phe Val Glu Gln Lys Tyr Glu Leu Gly Ala
145      150      155      160
Ala Leu Phe Ile Gly Trp Ala Gly Ala Ser Leu Cys Ile Ile Gly Gly
      165      170      175
Val Ile Phe Cys Phe Ser Ile Ser Asp Asn Asn Lys Thr Pro Arg Tyr
      180      185      190
Thr Tyr Asn Gly Ala Thr Ser Val Met Ser Ser Arg Thr Lys Tyr His
      195      200      205
Gly Gly Glu Asp Phe Lys Thr Thr Asn Pro Ser Lys Gln Phe Asp Lys
      210      215      220
Asn Ala Tyr Val
225

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<210> 50
<211> 1024
<212> DNA
<213> Homo sapiens

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<400> 50
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gcaactcaag acacctgcag cagggcgtga gaaaaagtaa aagaccagta ttttcacatt 180
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tcgcttgctt ctttgccttt ttctctgctg ggtttttgat tgtggccacc tggactgact 360
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ctttggtttt gcacaatata tttcttggtg tccaatataa atttggttgg tcctgttggc 780
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cagccgcggg tgtttccatg gccaaagtc actcagcccc tcgcacagag acggcctaaa 960
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aatc 1024

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<210> 51
<211> 305
<212> PRT
<213> Homo sapiens

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<400> 51
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Tyr Cys Asn Ser Arg His Leu Gln Gln Gly Val Arg Lys Ser Lys Arg
      20      25      30
Pro Val Phe Ser His Cys Gln Val Pro Glu Thr Gln Lys Thr Asp Thr
      35      40      45
Arg His Leu Ser Gly Ala Arg Ala Gly Val Cys Pro Cys Cys His Pro
      50      55      60

```

59

Asp Gly Leu Leu Ala Thr Met Arg Asp Leu Leu Gln Tyr Ile Ala Cys  
 65 70 75 80  
 Phe Phe Ala Phe Phe Ser Ala Gly Phe Leu Ile Val Ala Thr Trp Thr  
 85 90 95  
 Asp Cys Trp Met Val Asn Ala Asp Asp Ser Leu Glu Val Ser Thr Lys  
 100 105 110  
 Cys Arg Gly Leu Trp Trp Glu Cys Val Thr Asn Ala Phe Asp Gly Ile  
 115 120 125  
 Arg Thr Cys Asp Glu Tyr Asp Ser Ile Leu Ala Glu His Pro Leu Lys  
 130 135 140  
 Leu Val Val Thr Arg Ala Leu Met Ile Thr Ala Asp Ile Leu Ala Gly  
 145 150 155 160  
 Phe Gly Phe Leu Thr Leu Leu Leu Gly Leu Asp Cys Val Lys Phe Leu  
 165 170 175  
 Pro Asp Glu Pro Tyr Ile Lys Val Arg Ile Cys Phe Val Ala Gly Ala  
 180 185 190  
 Thr Leu Leu Ile Ala Gly Thr Pro Gly Ile Ile Gly Ser Val Trp Tyr  
 195 200 205  
 Ala Val Asp Val Tyr Val Glu Arg Ser Thr Leu Val Leu His Asn Ile  
 210 215 220  
 Phe Leu Gly Ile Gln Tyr Lys Phe Gly Trp Ser Cys Trp Leu Gly Met  
 225 230 235 240  
 Ala Gly Ser Leu Gly Cys Phe Leu Ala Gly Ala Val Leu Thr Cys Cys  
 245 250 255  
 Leu Tyr Leu Phe Lys Asp Val Gly Pro Glu Arg Asn Tyr Pro Tyr Ser  
 260 265 270  
 Leu Arg Lys Ala Tyr Ser Ala Ala Gly Val Ser Met Ala Lys Ser Tyr  
 275 280 285  
 Ser Ala Pro Arg Thr Glu Thr Ala Lys Met Tyr Ala Val Asp Thr Arg  
 290 295 300  
 Val  
 305

&lt;210&gt; 52

&lt;211&gt; 1665

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 52

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 acggcccccag cagccggatc ccctcagcct tccagggtcct caactcccgt ggacgctgaa 180  
 caatggcctc catggggcta caggtaatgg gcatcgcgct ggccgtcctg ggctgggtgg 240  
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 ttgtcacctc gcagaccatc tgggagggcc tatggatgaa ctgcgtggtg cagagcaccg 360  
 gccagatgca gtgcaagggtg tacgactcgc tgctggcact gccgcaggac ctgcaggcgg 420  
 cccgcgcctc cgtcatcatc agcatcatcg tggctgctct gggcgtgctg ctgtccgtgg 480  
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 cccacaacat catccaagac ttctacaatc cgtcgttggtg ctccgggcag aagcgggaga 660  
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60

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<210> 53  
 <211> 209  
 <212> PRT  
 <213> Homo sapiens

<400> 53

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			20					25					30		
Thr	Ala	Phe	Ile	Gly	Ser	Asn	Ile	Val	Thr	Ser	Gln	Thr	Ile	Trp	Glu
		35				40					45				
Gly	Leu	Trp	Met	Asn	Cys	Val	Val	Gln	Ser	Thr	Gly	Gln	Met	Gln	Cys
	50				55						60				
Lys	Val	Tyr	Asp	Ser	Leu	Leu	Ala	Leu	Pro	Gln	Asp	Leu	Gln	Ala	Ala
65					70					75				80	
Arg	Ala	Leu	Val	Ile	Ile	Ser	Ile	Ile	Val	Ala	Ala	Leu	Gly	Val	Leu
			85						90					95	
Leu	Ser	Val	Val	Gly	Gly	Lys	Cys	Thr	Asn	Cys	Leu	Glu	Asp	Glu	Ser
			100					105					110		
Ala	Lys	Ala	Lys	Thr	Met	Ile	Val	Ala	Gly	Val	Val	Phe	Leu	Leu	Ala
		115				120						125			
Gly	Leu	Met	Val	Ile	Val	Pro	Val	Ser	Trp	Thr	Ala	His	Asn	Ile	Ile
	130					135					140				
Gln	Asp	Phe	Tyr	Asn	Pro	Leu	Val	Ala	Ser	Gly	Gln	Lys	Arg	Glu	Met
145					150					155				160	
Gly	Ala	Ser	Leu	Tyr	Val	Gly	Trp	Ala	Ala	Ser	Gly	Leu	Leu	Leu	Leu
			165					170						175	
Gly	Gly	Gly	Leu	Leu	Cys	Cys	Asn	Cys	Pro	Pro	Arg	Thr	Asp	Lys	Pro
			180					185					190		
Tyr	Ser	Ala	Lys	Tyr	Ser	Ala	Ala	Arg	Ser	Ala	Ala	Ala	Ser	Asn	Tyr
		195				200						205			

Val

<210> 54  
 <211> 3457  
 <212> DNA  
 <213> Homo sapiens

<220>  
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 <223> n = A,T,C or G

<400> 54

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<210> 55  
 <211> 1069  
 <212> PRT  
 <213> Homo sapiens

<400> 55

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      20           25           30
Trp Asp Tyr Ala Ser Asp His Gly Glu Lys Lys Leu Ile Ser Val Asp
      35           40           45
Thr Glu His Ser Asn Ile Tyr Leu Gln Asn Gly Pro Asp Arg Ile Gly
      50           55           60
Arg Leu Tyr Lys Lys Ala Leu Tyr Leu Gln Tyr Thr Asp Glu Thr Phe
 65           70           75           80
Arg Thr Thr Ile Glu Lys Pro Val Trp Leu Gly Phe Leu Gly Pro Ile
      85           90           95
Ile Lys Ala Glu Thr Gly Asp Lys Val Tyr Val His Leu Lys Asn Leu
      100          105          110
Ala Ser Arg Pro Tyr Thr Phe His Ser His Gly Ile Thr Tyr Tyr Lys
      115          120          125
Glu His Glu Gly Ala Ile Tyr Pro Asp Asn Thr Thr Asp Phe Gln Arg
      130          135          140
Ala Asp Asp Lys Val Tyr Pro Gly Glu Gln Tyr Thr Tyr Met Leu Leu
 145          150          155          160
Ala Thr Glu Glu Gln Ser Pro Gly Glu Gly Asp Gly Asn Cys Val Thr
      165          170          175
Arg Ile Tyr His Ser His Ile Asp Ala Pro Lys Asp Ile Ala Ser Gly
      180          185          190
Leu Ile Gly Pro Leu Ile Ile Cys Lys Lys Asp Ser Leu Asp Lys Glu
      195          200          205
Lys Glu Lys His Ile Asp Arg Glu Phe Val Val Met Phe Ser Val Val
      210          215          220
Asp Glu Asn Phe Ser Trp Tyr Leu Glu Asp Asn Ile Lys Thr Tyr Cys
 225          230          235          240
Ser Glu Pro Glu Lys Val Asp Lys Asp Asn Glu Asp Phe Gln Glu Ser
      245          250          255
Asn Arg Met Tyr Ser Val Asn Gly Tyr Thr Phe Gly Ser Leu Pro Gly
      260          265          270
Leu Ser Met Cys Ala Glu Asp Arg Val Lys Trp Tyr Leu Phe Gly Met
      275          280          285
Gly Asn Glu Val Asp Val His Ala Ala Phe Phe His Gly Gln Ala Leu
      290          295          300
Thr Asn Lys Asn Tyr Arg Ile Asp Thr Ile Asn Leu Phe Pro Ala Thr
 305          310          315          320
Leu Phe Asp Ala Tyr Met Val Ala Gln Asn Pro Gly Glu Trp Met Leu
      325          330          335
Ser Cys Gln Asn Leu Asn His Leu Lys Ala Gly Leu Gln Ala Phe Phe
      340          345          350
Gln Val Gln Glu Cys Asn Lys Ser Ser Ser Lys Asp Asn Ile Arg Gly
      355          360          365
Lys His Val Arg His Tyr Tyr Ile Ala Ala Glu Glu Ile Ile Trp Asn
      370          375          380
Tyr Ala Pro Ser Gly Ile Asp Ile Phe Thr Lys Glu Asn Leu Thr Ala
 385          390          395          400
Pro Gly Ser Asp Ser Ala Val Phe Phe Glu Gln Gly Thr Thr Arg Ile
  
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				405					410					415			
Gly	Gly	Ser	Tyr	Lys	Lys	Leu	Val	Tyr	Arg	Glu	Tyr	Thr	Asp	Ala	Ser		
			420					425					430				
Phe	Thr	Asn	Arg	Lys	Glu	Arg	Gly	Pro	Glu	Glu	Glu	His	Leu	Gly	Ile		
		435					440					445					
Leu	Gly	Pro	Val	Ile	Trp	Ala	Glu	Val	Gly	Asp	Thr	Ile	Arg	Val	Thr		
	450					455					460						
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Arg	Phe	Asn	Lys	Asn	Asn	Glu	Gly	Thr	Tyr	Tyr	Ser	Pro	Asn	Tyr	Asn		
			485					490						495			
Pro	Gln	Ser	Arg	Ser	Val	Pro	Pro	Ser	Ala	Ser	His	Val	Ala	Pro	Thr		
		500						505					510				
Glu	Thr	Phe	Thr	Tyr	Glu	Trp	Thr	Val	Pro	Lys	Glu	Val	Gly	Pro	Thr		
	515						520					525					
Asn	Ala	Asp	Pro	Val	Cys	Leu	Ala	Lys	Met	Tyr	Tyr	Ser	Ala	Val	Asp		
	530					535					540						
Pro	Thr	Lys	Asp	Ile	Phe	Thr	Gly	Leu	Ile	Gly	Pro	Met	Lys	Ile	Cys		
545				550						555					560		
Lys	Lys	Gly	Ser	Leu	His	Ala	Asn	Gly	Arg	Gln	Lys	Asp	Val	Asp	Lys		
			565					570						575			
Glu	Phe	Tyr	Leu	Phe	Pro	Thr	Val	Phe	Asp	Glu	Asn	Glu	Ser	Leu	Leu		
		580						585					590				
Leu	Glu	Asp	Asn	Ile	Arg	Met	Phe	Thr	Thr	Ala	Pro	Asp	Gln	Val	Asp		
	595					600						605					
Lys	Glu	Asp	Glu	Asp	Phe	Gln	Glu	Ser	Asn	Lys	Met	His	Ser	Met	Asn		
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Asp	Thr	Ala	Asn	Leu	Phe	Pro	Gln	Thr	Ser	Leu	Thr	Leu	His	Met	Trp		
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Pro	Asp	Thr	Glu	Gly	Thr	Phe	Asn	Val	Glu	Cys	Leu	Thr	Thr	Asp	His		
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Gln	Ser	Glu	Asp	Ser	Thr	Phe	Tyr	Leu	Gly	Glu	Arg	Thr	Tyr	Tyr	Ile		
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		740					745						750				
Lys	Glu	Leu	His	His	Leu	Gln	Glu	Gln	Asn	Val	Ser	Asn	Ala	Phe	Leu		
	755					760						765					
Asp	Lys	Gly	Glu	Phe	Tyr	Ile	Gly	Ser	Lys	Tyr	Lys	Lys	Val	Val	Tyr		
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		820						825					830				
Ser	Ile	His	Ala	His	Gly	Val	Gln	Thr	Glu	Ser	Ser	Thr	Val	Thr	Pro		
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Thr	Leu	Pro	Gly	Glu	Thr	Leu	Thr	Tyr	Val	Trp	Lys	Ile	Pro	Glu	Arg		
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Ser	Gly	Ala	Gly	Thr	Glu	Asp	Ser	Ala	Cys	Ile	Pro	Trp	Ala	Tyr	Tyr		

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Leu Ile Val Cys Arg Arg Pro Tyr	Leu Lys Val Phe Asn Pro Arg Arg					
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Lys Leu Glu Phe Ala Leu Leu Phe	Leu Val Phe Asp Glu Asn Glu Ser					
	915		920			925
Trp Tyr Leu Asp Asp Asn Ile Lys Thr Tyr Ser	Asp His Pro Glu Lys					
	930		935			940
Val Asn Lys Asp Asp Glu Glu Phe Ile Glu Ser	Asn Lys Met His Ala					
	945		950			955
Ile Asn Gly Arg Met Phe Gly Asn Leu Gln Gly	Leu Thr Met His Val					
	965		970			975
Gly Asp Glu Val Asn Trp Tyr Leu Met Gly Met	Gly Asn Glu Ile Asp					
	980		985			990
Leu His Thr Val His Phe His Gly His Ser Phe	Gln Tyr Lys His Arg					
	995		1000			1005
Gly Val Tyr Ser Ser Asp Val Phe Asp Ile Phe	Pro Gly Thr Tyr Gln					
	1010		1015			1020
Thr Leu Glu Met Phe Pro Arg Thr Pro Gly Ile Trp Leu Leu His Cys						
	1025		1030			1035
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 <212> DNA  
 <213> Homo sapiens

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 cagaatgtat tctgtgaatg gatacacttt tggaagtctc ccaggactct ccatgtgtgc 180  
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 tcctgctacc ctgtttgatg cttatatggg ggcccagaac cctggagaat ggatgctcag 360  
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&lt;210&gt; 57

&lt;211&gt; 852

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 57 .

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      20          25          30
Asn Glu Asp Phe Gln Glu Ser Asn Arg Met Tyr Ser Val Asn Gly Tyr
      35          40          45
Thr Phe Gly Ser Leu Pro Gly Leu Ser Met Cys Ala Glu Asp Arg Val
      50          55          60
Lys Trp Tyr Leu Phe Gly Met Gly Asn Glu Val Asp Val His Ala Ala
      65          70          75          80
Phe Phe His Gly Gln Ala Leu Thr Asn Lys Asn Tyr Arg Ile Asp Thr
      85          90          95
Ile Asn Leu Phe Pro Ala Thr Leu Phe Asp Ala Tyr Met Val Ala Gln
      100          105          110
Asn Pro Gly Glu Trp Met Leu Ser Cys Gln Asn Leu Asn His Leu Lys
      115          120          125
Ala Gly Leu Gln Ala Phe Phe Gln Val Gln Glu Cys Asn Lys Ser Ser
      130          135          140
Ser Lys Asp Asn Ile Arg Gly Lys His Val Arg His Tyr Tyr Ile Ala
      145          150          155          160
Ala Glu Glu Ile Ile Trp Asn Tyr Ala Pro Ser Gly Ile Asp Ile Phe
      165          170          175
Thr Lys Glu Asn Leu Thr Ala Pro Gly Ser Asp Ser Ala Val Phe Phe
      180          185          190
Glu Gln Gly Thr Thr Arg Ile Gly Gly Ser Tyr Lys Lys Leu Val Tyr
      195          200          205
Arg Glu Tyr Thr Asp Ala Ser Phe Thr Asn Arg Lys Glu Arg Gly Pro
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Glu Glu Glu His Leu Gly Ile Leu Gly Pro Val Ile Trp Ala Glu Val

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			260					265					270	Thr
Tyr	Tyr	Ser	Pro	Asn	Tyr	Asn	Pro	Gln	Ser	Arg	Ser	Val	Pro	Pro
		275					280					285		Ser
Ala	Ser	His	Val	Ala	Pro	Thr	Glu	Thr	Phe	Thr	Tyr	Glu	Trp	Thr
	290					295					300			Val
Pro	Lys	Glu	Val	Gly	Pro	Thr	Asn	Ala	Asp	Pro	Val	Cys	Leu	Ala
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Met	Tyr	Tyr	Ser	Ala	Val	Asp	Pro	Thr	Lys	Asp	Ile	Phe	Thr	Gly
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Ile	Gly	Pro	Met	Lys	Ile	Cys	Lys	Lys	Gly	Ser	Leu	His	Ala	Asn
			340						345				350	Gly
Arg	Gln	Lys	Asp	Val	Asp	Lys	Glu	Phe	Tyr	Leu	Phe	Pro	Thr	Val
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Asp	Glu	Asn	Glu	Ser	Leu	Leu	Glu	Asp	Asn	Ile	Arg	Met	Phe	Thr
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Thr	Ala	Pro	Asp	Gln	Val	Asp	Lys	Glu	Asp	Glu	Asp	Phe	Gln	Glu
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Asn	Lys	Met	His	Ser	Met	Asn	Gly	Phe	Met	Tyr	Gly	Asn	Gln	Pro
			405						410				415	Gly
Leu	Thr	Met	Cys	Lys	Gly	Asp	Ser	Val	Val	Trp	Tyr	Leu	Phe	Ser
		420						425					430	Ala
Gly	Asn	Glu	Ala	Asp	Val	His	Gly	Ile	Tyr	Phe	Ser	Gly	Asn	Thr
	435						440					445		Tyr
Leu	Trp	Arg	Gly	Glu	Arg	Arg	Asp	Thr	Ala	Asn	Leu	Phe	Pro	Gln
	450					455					460			Thr
Ser	Leu	Thr	Leu	His	Met	Trp	Pro	Asp	Thr	Glu	Gly	Thr	Phe	Asn
465					470					475				Val
Glu	Cys	Leu	Thr	Thr	Asp	His	Tyr	Thr	Gly	Gly	Met	Lys	Gln	Lys
			485						490					Tyr
Thr	Val	Asn	Gln	Cys	Arg	Arg	Gln	Ser	Glu	Asp	Ser	Thr	Phe	Tyr
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Gly	Glu	Arg	Thr	Tyr	Tyr	Ile	Ala	Ala	Val	Glu	Val	Glu	Trp	Asp
	515						520					525		Tyr
Ser	Pro	Gln	Arg	Glu	Trp	Glu	Lys	Glu	Leu	His	His	Leu	Gln	Glu
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Asn	Val	Ser	Asn	Ala	Phe	Leu	Asp	Lys	Gly	Glu	Phe	Tyr	Ile	Gly
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Lys	Tyr	Lys	Lys	Val	Val	Tyr	Arg	Gln	Tyr	Thr	Asp	Ser	Thr	Phe
			565						570					Arg
Val	Pro	Val	Glu	Arg	Lys	Ala	Glu	Glu	Glu	His	Leu	Gly	Ile	Leu
		580						585					590	Gly
Pro	Gln	Leu	His	Ala	Asp	Val	Gly	Asp	Lys	Val	Lys	Ile	Ile	Phe
	595						600					605		Lys
Asn	Met	Ala	Thr	Arg	Pro	Tyr	Ser	Ile	His	Ala	His	Gly	Val	Gln
	610					615					620			Thr
Glu	Ser	Ser	Thr	Val	Thr	Pro	Thr	Leu	Pro	Gly	Glu	Thr	Leu	Thr
625					630					635				Tyr
Val	Trp	Lys	Ile	Pro	Glu	Arg	Ser	Gly	Ala	Gly	Thr	Glu	Asp	Ser
			645						650					Ala
Cys	Ile	Pro	Trp	Ala	Tyr	Tyr	Ser	Thr	Val	Asp	Gln	Val	Lys	Asp
		660						665					670	Leu
Tyr	Ser	Gly	Leu	Ile	Gly	Pro	Leu	Ile	Val	Cys	Arg	Arg	Pro	Tyr
	675					680					685			Leu
Lys	Val	Phe	Asn	Pro	Arg	Arg	Lys	Leu	Glu	Phe	Ala	Leu	Leu	Phe

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Tyr Ser Asp His Pro Glu Lys Val Asn Lys Asp	Asp Glu Glu Phe Ile	720
	725	730
Glu Ser Asn Lys Met His Ala Ile Asn Gly Arg	Met Phe Gly Asn Leu	735
	740	745
Gln Gly Leu Thr Met His Val Gly Asp Glu Val	Asn Trp Tyr Leu Met	750
	755	760
Gly Met Gly Asn Glu Ile Asp Leu His Thr Val	His Phe His Gly His	765
	770	775
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785	790	795
Ile Phe Pro Gly Thr Tyr Gln Thr Leu Glu Met	Phe Pro Arg Thr Pro	800
	805	810
Gly Ile Trp Leu Leu His Cys His Val Thr Asp	His Ile His Ala Gly	815
	820	825
Met Glu Thr Thr Tyr Thr Val Leu Gln Asn Glu	Gly Glu Tyr Pro Asp	830
	835	840
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&lt;210&gt; 58

&lt;211&gt; 3321

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 58

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&lt;210&gt; 59

&lt;211&gt; 1065

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 59

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Trp Asp Tyr Ala Ser Asp His Gly Glu Lys Lys Leu Ile Ser Val Asp
      35             40             45
Thr Glu His Ser Asn Ile Tyr Leu Gln Asn Gly Pro Asp Arg Ile Gly
      50             55             60
Arg Leu Tyr Lys Lys Ala Leu Tyr Leu Gln Tyr Thr Asp Glu Thr Phe
      65             70             75             80
Arg Thr Thr Ile Glu Lys Pro Val Trp Leu Gly Phe Leu Gly Pro Ile
      85             90             95
Ile Lys Ala Glu Thr Gly Asp Lys Val Tyr Val His Leu Lys Asn Leu
      100            105            110
Ala Ser Arg Pro Tyr Thr Phe His Ser His Gly Ile Thr Tyr Tyr Lys
      115            120            125
Glu His Glu Gly Ala Ile Tyr Pro Asp Asn Thr Thr Asp Phe Gln Arg
      130            135            140
Ala Asp Asp Lys Val Tyr Pro Gly Glu Gln Tyr Thr Tyr Met Leu Leu
      145            150            155            160
Ala Thr Glu Glu Gln Ser Pro Gly Glu Gly Asp Gly Asn Cys Val Thr
      165            170            175
Arg Ile Tyr His Ser His Ile Asp Ala Pro Lys Asp Ile Ala Ser Gly
      180            185            190

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Leu Ile Gly Pro Leu Ile Ile Cys Lys Lys Asp Ser Leu Asp Lys Glu  
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 Lys Glu Lys His Ile Asp Arg Glu Phe Val Val Met Phe Ser Val Val  
 210 215 220  
 Asp Glu Asn Phe Ser Trp Tyr Leu Glu Asp Asn Ile Lys Thr Tyr Cys  
 225 230 235 240  
 Ser Glu Pro Glu Lys Val Asp Lys Asp Asn Glu Asp Phe Gln Glu Ser  
 245 250 255  
 Asn Arg Met Tyr Ser Val Asn Gly Tyr Thr Phe Gly Ser Leu Pro Gly  
 260 265 270  
 Leu Ser Met Cys Ala Glu Asp Arg Val Lys Trp Tyr Leu Phe Gly Met  
 275 280 285  
 Gly Asn Glu Val Asp Val His Ala Ala Phe Phe His Gly Gln Ala Leu  
 290 295 300  
 Thr Asn Lys Asn Tyr Arg Ile Asp Thr Ile Asn Leu Phe Pro Ala Thr  
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 Leu Phe Asp Ala Tyr Met Val Ala Gln Asn Pro Gly Glu Trp Met Leu  
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 Ser Cys Gln Asn Leu Asn His Leu Lys Ala Gly Leu Gln Ala Phe Phe  
 340 345 350  
 Gln Val Gln Glu Cys Asn Lys Ser Ser Ser Lys Asp Asn Ile Arg Gly  
 355 360 365  
 Lys His Val Arg His Tyr Tyr Ile Ala Ala Glu Glu Ile Ile Trp Asn  
 370 375 380  
 Tyr Ala Pro Ser Gly Ile Asp Ile Phe Thr Lys Glu Asn Leu Thr Ala  
 385 390 395 400  
 Pro Gly Ser Asp Ser Ala Val Phe Phe Glu Gln Gly Thr Thr Arg Ile  
 405 410 415  
 Gly Gly Ser Tyr Lys Lys Leu Val Tyr Arg Glu Tyr Thr Asp Ala Ser  
 420 425 430  
 Phe Thr Asn Arg Lys Glu Arg Gly Pro Glu Glu Glu His Leu Gly Ile  
 435 440 445  
 Leu Gly Pro Val Ile Trp Ala Glu Val Gly Asp Thr Ile Arg Val Thr  
 450 455 460  
 Phe His Asn Lys Gly Ala Tyr Pro Leu Ser Ile Glu Pro Ile Gly Val  
 465 470 475 480  
 Arg Phe Asn Lys Asn Asn Glu Gly Thr Tyr Tyr Ser Pro Asn Tyr Asn  
 485 490 495  
 Pro Gln Ser Arg Ser Val Pro Pro Ser Ala Ser His Val Ala Pro Thr  
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 Glu Thr Phe Thr Tyr Glu Trp Thr Val Pro Lys Glu Val Gly Pro Thr  
 515 520 525  
 Asn Ala Asp Pro Val Cys Leu Ala Lys Met Tyr Tyr Ser Ala Val Asp  
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 Pro Thr Lys Asp Ile Phe Thr Gly Leu Ile Gly Pro Met Lys Ile Cys  
 545 550 555 560  
 Lys Lys Gly Ser Leu His Ala Asn Gly Arg Gln Lys Asp Val Asp Lys  
 565 570 575  
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 580 585 590  
 Leu Glu Asp Asn Ile Arg Met Phe Thr Thr Ala Pro Asp Gln Val Asp  
 595 600 605  
 Lys Glu Asp Glu Asp Phe Gln Glu Ser Asn Lys Met His Ser Met Asn  
 610 615 620  
 Gly Phe Met Tyr Gly Asn Gln Pro Gly Leu Thr Met Cys Lys Gly Asp  
 625 630 635 640  
 Ser Val Val Trp Tyr Leu Phe Ser Ala Gly Asn Glu Ala Asp Val His  
 645 650 655

Gly Ile Tyr Phe Ser Gly Asn Thr Tyr Leu Trp Arg Gly Glu Arg Arg  
                   660                  665                  670  
 Asp Thr Ala Asn Leu Phe Pro Gln Thr Ser Leu Thr Leu His Met Trp  
                   675                  680                  685  
 Pro Asp Thr Glu Gly Thr Phe Asn Val Glu Cys Leu Thr Thr Asp His  
                   690                  695                  700  
 Tyr Thr Gly Gly Met Lys Gln Lys Tyr Thr Val Asn Gln Cys Arg Arg  
 705                  710                  715                  720  
 Gln Ser Glu Asp Ser Thr Phe Tyr Leu Gly Glu Arg Thr Tyr Tyr Ile  
                   725                  730                  735  
 Ala Ala Val Glu Val Glu Trp Asp Tyr Ser Pro Gln Arg Glu Trp Glu  
                   740                  745                  750  
 Lys Glu Leu His His Leu Gln Glu Gln Asn Val Ser Asn Ala Phe Leu  
                   755                  760                  765  
 Asp Lys Gly Glu Phe Tyr Ile Gly Ser Lys Tyr Lys Lys Val Val Tyr  
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 Arg Gln Tyr Thr Asp Ser Thr Phe Arg Val Pro Val Glu Arg Lys Ala  
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 Glu Glu Glu His Leu Gly Ile Leu Gly Pro Gln Leu His Ala Asp Val  
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                   820                  825                  830  
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                   835                  840                  845  
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 Ser Gly Ala Gly Thr Glu Asp Ser Ala Cys Ile Pro Trp Ala Tyr Tyr  
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 Ser Thr Val Asp Gln Val Lys Asp Leu Tyr Ser Gly Leu Ile Gly Pro  
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                   900                  905                  910  
 Lys Leu Glu Phe Ala Leu Leu Phe Leu Val Phe Asp Glu Asn Glu Ser  
                   915                  920                  925  
 Trp Tyr Leu Asp Asp Asn Ile Lys Thr Tyr Ser Asp His Pro Glu Lys  
 930                  935                  940  
 Val Asn Lys Asp Asp Glu Glu Phe Ile Glu Ser Asn Lys Met His Ala  
 945                  950                  955                  960  
 Ile Asn Gly Arg Met Phe Gly Asn Leu Gln Gly Leu Thr Met His Val  
                   965                  970                  975  
 Gly Asp Glu Val Asn Trp Tyr Leu Met Gly Met Gly Asn Glu Ile Asp  
                   980                  985                  990  
 Leu His Thr Val His Phe His Gly His Ser Phe Gln Tyr Lys His Arg  
                   995                  1000                  1005  
 Gly Val Tyr Ser Ser Asp Val Phe Asp Ile Phe Pro Gly Thr Tyr Gln  
 1010                  1015                  1020  
 Thr Leu Glu Met Phe Pro Arg Thr Pro Gly Ile Trp Leu Leu His Cys  
 1025                  1030                  1035                  1040  
 His Val Thr Asp His Ile His Ala Gly Met Glu Thr Thr Tyr Thr Val  
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                   1060                  1065

&lt;210&gt; 60

&lt;211&gt; 3881

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

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<400> 60

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gcctctgacc atggggaaaa gaaacttatt tctgttgaca cggaacattc caatatctat 240
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cctgataaca ccacagatth tcaaagagca gatgacaaag tatatccagg agagcagtat 540
acatacatgt tgcttgccac tgaagaacaa agtcctgggg aaggagatgg caattgtgtg 600
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&lt;210&gt; 61

&lt;211&gt; 1090

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 61

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Met Lys Ile Leu Ile Leu Gly Ile Phe Leu Phe Leu Cys Ser Thr Pro
  1             5             10             15
Ala Trp Ala Lys Glu Lys His Tyr Tyr Ile Gly Ile Ile Glu Thr Thr
      20             25             30
Trp Asp Tyr Ala Ser Asp His Gly Glu Lys Lys Leu Ile Ser Val Asp
      35             40             45
Thr Glu His Ser Asn Ile Tyr Leu Gln Asn Gly Pro Asp Arg Ile Gly
      50             55             60
Arg Leu Tyr Lys Lys Ala Leu Tyr Leu Gln Tyr Thr Asp Glu Thr Phe
      65             70             75             80
Arg Thr Thr Ile Glu Lys Pro Val Trp Leu Gly Phe Leu Gly Pro Ile
      85             90             95
Ile Lys Ala Glu Thr Gly Asp Lys Val Tyr Val His Leu Lys Asn Leu
      100            105            110
Ala Ser Arg Pro Tyr Thr Phe His Ser His Gly Ile Thr Tyr Tyr Lys
      115            120            125
Glu His Glu Gly Ala Ile Tyr Pro Asp Asn Thr Thr Asp Phe Gln Arg
      130            135            140
Ala Asp Asp Lys Val Tyr Pro Gly Glu Gln Tyr Thr Tyr Met Leu Leu
      145            150            155            160
Ala Thr Glu Glu Gln Ser Pro Gly Glu Gly Asp Gly Asn Cys Val Thr
      165            170            175
Arg Ile Tyr His Ser His Ile Asp Ala Pro Lys Asp Ile Ala Ser Gly
      180            185            190
Leu Ile Gly Pro Leu Ile Ile Cys Lys Lys Asp Ser Leu Asp Lys Glu
      195            200            205
Lys Glu Lys His Ile Asp Arg Glu Phe Val Val Met Phe Ser Val Val
      210            215            220
Asp Glu Asn Phe Ser Trp Tyr Leu Glu Asp Asn Ile Lys Thr Tyr Cys
      225            230            235            240
Ser Glu Pro Glu Lys Val Asp Lys Asp Asn Glu Asp Phe Gln Glu Ser
      245            250            255
Asn Arg Met Tyr Ser Val Asn Gly Tyr Thr Phe Gly Ser Leu Pro Gly
      260            265            270
Leu Ser Met Cys Ala Glu Asp Arg Val Lys Trp Tyr Leu Phe Gly Met
      275            280            285
Gly Asn Glu Val Asp Val His Ala Ala Phe Phe His Gly Gln Ala Leu

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290		295		300
Thr Asn Lys Asn Tyr Arg Ile Asp Thr Ile Asn Leu Phe Pro Ala Thr				
305		310		320
Leu Phe Asp Ala Tyr Met Val Ala Gln Asn Pro Gly Glu Trp Met Leu				
	325		330	335
Ser Cys Gln Asn Leu Asn His Leu Lys Ala Gly Leu Gln Ala Phe Phe				
	340		345	350
Gln Val Gln Glu Cys Asn Lys Ser Ser Ser Lys Asp Asn Ile Arg Gly				
	355		360	365
Lys His Val Arg His Tyr Tyr Ile Ala Ala Glu Glu Ile Ile Trp Asn				
	370		375	380
Tyr Ala Pro Ser Gly Ile Asp Ile Phe Thr Lys Glu Asn Leu Thr Ala				
385		390		400
Pro Gly Ser Asp Ser Ala Val Phe Phe Glu Gln Gly Thr Thr Arg Ile				
	405		410	415
Gly Gly Ser Tyr Lys Lys Leu Val Tyr Arg Glu Tyr Thr Asp Ala Ser				
	420		425	430
Phe Thr Asn Arg Lys Glu Arg Gly Pro Glu Glu Glu His Leu Gly Ile				
	435		440	445
Leu Gly Pro Val Ile Trp Ala Glu Val Gly Asp Thr Ile Arg Val Thr				
	450		455	460
Phe His Asn Lys Gly Ala Tyr Pro Leu Ser Ile Glu Pro Ile Gly Val				
465		470		480
Arg Phe Asn Lys Asn Asn Glu Gly Thr Tyr Tyr Ser Pro Asn Tyr Asn				
	485		490	495
Pro Gln Ser Arg Ser Val Pro Pro Ser Ala Ser His Val Ala Pro Thr				
	500		505	510
Glu Thr Phe Thr Tyr Glu Trp Thr Val Pro Lys Glu Val Gly Pro Thr				
	515		520	525
Asn Ala Asp Pro Val Cys Leu Ala Lys Met Tyr Tyr Ser Ala Val Asp				
	530		535	540
Pro Thr Lys Asp Ile Phe Thr Gly Leu Ile Gly Pro Met Lys Ile Cys				
545		550		560
Lys Lys Gly Ser Leu His Ala Asn Gly Arg Gln Lys Asp Val Asp Lys				
	565		570	575
Glu Phe Tyr Leu Phe Pro Thr Val Phe Asp Glu Asn Glu Ser Leu Leu				
	580		585	590
Leu Glu Asp Asn Ile Arg Met Phe Thr Thr Ala Pro Asp Gln Val Asp				
	595		600	605
Lys Glu Asp Glu Asp Phe Gln Glu Ser Asn Lys Met His Ser Met Asn				
	610		615	620
Gly Phe Met Tyr Gly Asn Gln Pro Gly Leu Thr Met Cys Lys Gly Asp				
625		630		640
Ser Val Val Trp Tyr Leu Phe Ser Ala Gly Asn Glu Ala Asp Val His				
	645		650	655
Gly Ile Tyr Phe Ser Gly Asn Thr Tyr Leu Trp Arg Gly Glu Arg Arg				
	660		665	670
Asp Thr Ala Asn Leu Phe Pro Gln Thr Ser Leu Thr Leu His Met Trp				
	675		680	685
Pro Asp Thr Glu Gly Thr Phe Asn Val Glu Cys Leu Thr Thr Asp His				
	690		695	700
Tyr Thr Gly Gly Met Lys Gln Lys Tyr Thr Val Asn Gln Cys Arg Arg				
705		710		720
Gln Ser Glu Asp Ser Thr Phe Tyr Leu Gly Glu Arg Thr Tyr Tyr Ile				
	725		730	735
Ala Ala Val Glu Val Glu Trp Asp Tyr Ser Pro Gln Arg Glu Trp Glu				
	740		745	750
Lys Glu Leu His His Leu Gln Glu Gln Asn Val Ser Asn Ala Phe Leu				

755	760	765
Asp Lys Gly Glu Phe Tyr Ile	Gly Ser Lys Tyr	Lys Lys Val Val Tyr
770	775	780
Arg Gln Tyr Thr Asp Ser Thr Phe Arg Val	Pro Val Glu Arg Lys Ala	
785	790	795
Glu Glu Glu His Leu Gly Ile Leu Gly Pro Gln Leu His Ala Asp Val		
805	810	815
Gly Asp Lys Val Lys Ile Ile Phe Lys Asn Met Ala Thr Arg Pro Tyr		
820	825	830
Ser Ile His Ala His Gly Val Gln Thr Glu Ser Ser Thr Val Thr Pro		
835	840	845
Thr Leu Pro Gly Glu Thr Leu Thr Tyr Val Trp Lys Ile Pro Glu Arg		
850	855	860
Ser Gly Ala Gly Thr Glu Asp Ser Ala Cys Ile Pro Trp Ala Tyr Tyr		
865	870	875
Ser Thr Val Asp Gln Val Lys Asp Leu Tyr Ser Gly Leu Ile Gly Pro		
885	890	895
Leu Ile Val Cys Arg Arg Pro Tyr Leu Lys Val Phe Asn Pro Arg Arg		
900	905	910
Lys Leu Glu Phe Ala Leu Leu Phe Leu Val Phe Asp Glu Asn Glu Ser		
915	920	925
Trp Tyr Leu Asp Asp Asn Ile Lys Thr Tyr Ser Asp His Pro Glu Lys		
930	935	940
Val Asn Lys Asp Asp Glu Glu Phe Ile Glu Ser Asn Lys Met His Ala		
945	950	955
Ile Asn Gly Arg Met Phe Gly Asn Leu Gln Gly Leu Thr Met His Val		
965	970	975
Gly Asp Glu Val Asn Trp Tyr Leu Met Gly Met Gly Asn Glu Ile Asp		
980	985	990
Leu His Thr Val His Phe His Gly His Ser Phe Gln Tyr Lys His Arg		
995	1000	1005
Gly Val Tyr Ser Ser Asp Val Phe Asp Ile Phe Pro Gly Thr Tyr Gln		
1010	1015	1020
Thr Leu Glu Met Phe Pro Arg Thr Pro Gly Ile Trp Leu Leu His Cys		
1025	1030	1035
His Val Thr Asp His Ile His Ala Gly Met Glu Thr Thr Tyr Thr Val		
1045	1050	1055
Leu Gln Asn Glu Ala Ser Ser Glu Thr His Arg Arg Ile Trp Asn Val		
1060	1065	1070
Ile Tyr Pro Ile Thr Val Ser Val Ile Ile Leu Phe Gln Ile Ser Thr		
1075	1080	1085
Lys Glu		
1090		

&lt;210&gt; 62

&lt;211&gt; 969

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 62

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ttaaaaaaa 969

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<210> 63  
 <211> 138  
 <212> PRT  
 <213> Homo sapiens

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20          25          30
Ala Val Ala Ala Ala Ser Lys Pro Ala Val Glu Ile Lys Gln Glu Gly
35          40          45
Asp Thr Phe Tyr Ile Lys Thr Ser Thr Thr Val Arg Thr Thr Glu Ile
50          55          60
Asn Phe Lys Val Gly Glu Phe Glu Glu Gln Thr Val Asp Gly Arg
65          70          75          80
Pro Cys Lys Ser Leu Val Lys Trp Glu Ser Glu Asn Lys Met Val Cys
85          90          95
Glu Gln Lys Leu Leu Lys Gly Glu Gly Pro Lys Thr Ser Trp Thr Arg
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Glu Leu Thr Asn Asp Gly Glu Leu Ile Leu Thr Met Thr Ala Asp Asp
115         120         125
Val Val Cys Thr Arg Val Tyr Val Arg Glu
130         135

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<210> 64  
 <211> 927  
 <212> DNA  
 <213> Homo sapiens

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<400> 64
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927

&lt;210&gt; 65

&lt;211&gt; 114

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 65

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Met Ser Ala Leu Ser Leu Leu Ile Leu Gly Leu Leu Thr Ala Val Pro
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Pro Ala Ser Cys Gln Gln Gly Leu Gly Asn Leu Gln Pro Trp Met Gln
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Gly Leu Ile Ala Val Ala Val Phe Leu Val Leu Val Ala Ile Ala Phe
      35           40           45
Ala Val Asn His Phe Trp Cys Gln Glu Glu Pro Glu Pro Ala His Met
      50           55           60
Ile Leu Thr Val Gly Asn Lys Ala Asp Gly Val Leu Val Gly Thr Asp
      65           70           75           80
Gly Arg Tyr Ser Ser Met Ala Ala Ser Phe Arg Ser Ser Glu His Glu
      85           90           95
Asn Ala Tyr Glu Asn Val Pro Glu Glu Glu Gly Lys Val Arg Ser Thr
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Pro Met

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&lt;210&gt; 66

&lt;211&gt; 3641

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 66

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&lt;210&gt; 67

&lt;211&gt; 482

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 67

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Met Asp Glu Gly Ile Pro His Leu Gln Glu Arg Gln Leu Leu Glu His
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Arg Asp Phe Ile Gly Leu Asp Tyr Ser Ser Leu Tyr Met Cys Lys Pro
          20          25          30
Lys Arg Ser Met Lys Arg Asp Asp Thr Lys Asp Thr Tyr Lys Leu Pro
          35          40          45
His Arg Leu Ile Glu Lys Lys Arg Arg Asp Arg Ile Asn Glu Cys Ile
          50          55          60
Ala Gln Leu Lys Asp Leu Leu Pro Glu His Leu Lys Leu Thr Thr Leu
65          70          75          80
Gly His Leu Glu Lys Ala Val Val Leu Glu Leu Thr Leu Lys His Leu
          85          90          95
Lys Ala Leu Thr Ala Leu Thr Glu Gln Gln His Gln Lys Ile Ile Ala
          100          105          110
Leu Gln Asn Gly Glu Arg Ser Leu Lys Ser Pro Ile Gln Ser Asp Leu
          115          120          125

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Asp Ala Phe His Ser Gly Phe Gln Thr Cys Ala Lys Glu Val Leu Gln  
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 Tyr Leu Ser Arg Phe Glu Ser Trp Thr Pro Arg Glu Pro Arg Cys Val  
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 Gln Leu Ile Asn His Leu His Ala Val Ala Thr Gln Phe Leu Pro Thr  
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 Pro Gln Leu Leu Thr Gln Gln Val Pro Leu Ser Lys Gly Thr Gly Ala  
 180 185 190  
 Pro Ser Ala Ala Gly Ser Ala Ala Ala Pro Cys Leu Glu Arg Ala Gly  
 195 200 205  
 Gln Lys Leu Glu Pro Leu Ala Tyr Cys Val Pro Val Ile Gln Arg Thr  
 210 215 220  
 Gln Pro Ser Ala Glu Leu Ala Ala Glu Asn Asp Thr Asp Thr Asp Ser  
 225 230 235 240  
 Gly Tyr Gly Gly Glu Ala Glu Ala Arg Pro Asp Arg Glu Lys Gly Lys  
 245 250 255  
 Gly Ala Gly Ala Ser Arg Val Thr Ile Lys Gln Glu Pro Pro Gly Glu  
 260 265 270  
 Asp Ser Pro Ala Pro Lys Arg Met Lys Leu Asp Ser Arg Gly Gly Gly  
 275 280 285  
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 325 330 335  
 Phe Pro Gln Pro Ala Ala Ala Ala Ala Pro Phe Cys Leu Pro Phe Cys  
 340 345 350  
 Phe Leu Ser Pro Ser Ala Ala Ala Ala Tyr Val Gln Pro Phe Leu Asp  
 355 360 365  
 Lys Ser Gly Leu Glu Lys Tyr Leu Tyr Pro Ala Ala Ala Ala Pro  
 370 375 380  
 Phe Pro Leu Leu Tyr Pro Gly Ile Pro Ala Pro Ala Ala Ala Ala  
 385 390 395 400  
 Ala Ala Ala Ala Ala Ala Ala Ala Ala Ala Ala Phe Pro Cys Leu Ser  
 405 410 415  
 Ser Val Leu Ser Pro Pro Pro Glu Lys Ala Gly Ala Ala Ala Ala Thr  
 420 425 430  
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 Pro His Gly Arg Thr His Leu Pro Phe Ala Gly Pro Arg Glu Pro Gly  
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 Ala Pro

&lt;210&gt; 68

&lt;211&gt; 3624

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 68

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<210> 69  
 <211> 341  
 <212> PRT  
 <213> Homo sapiens

<400> 69  
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 Ser Val Ala Gly Gln Val Cys Leu Ile Thr Gly Ala Gly Ser Gly Leu  
 35 40 45  
 Gly Arg Leu Phe Ala Leu Glu Phe Ala Arg Arg Arg Ala Leu Leu Val  
 50 55 60  
 Leu Trp Asp Ile Asn Thr Gln Ser Asn Glu Glu Thr Ala Gly Met Val  
 65 70 75 80  
 Arg His Ile Tyr Arg Asp Leu Glu Ala Ala Asp Ala Ala Ala Leu Gln  
 85 90 95  
 Ala Gly Asn Gly Glu Glu Glu Ile Leu Pro His Cys Asn Leu Gln Val  
 100 105 110  
 Phe Thr Tyr Thr Cys Asp Val Gly Lys Arg Glu Asn Val Tyr Leu Thr  
 115 120 125  
 Ala Glu Arg Val Arg Lys Glu Val Gly Glu Val Ser Val Leu Val Asn  
 130 135 140  
 Asn Ala Gly Val Val Ser Gly His His Leu Leu Glu Cys Pro Asp Glu  
 145 150 155 160  
 Leu Ile Glu Arg Thr Met Met Val Asn Cys His Ala His Phe Trp Thr  
 165 170 175  
 Thr Lys Ala Phe Leu Pro Thr Met Leu Glu Ile Asn His Gly His Ile  
 180 185 190  
 Val Thr Val Ala Ser Ser Leu Gly Leu Phe Ser Thr Ala Gly Val Glu  
 195 200 205  
 Asp Tyr Cys Ala Ser Lys Phe Gly Val Val Gly Phe His Glu Ser Leu  
 210 215 220  
 Ser His Glu Leu Lys Ala Ala Glu Lys Asp Gly Ile Lys Thr Thr Leu  
 225 230 235 240  
 Val Cys Pro Tyr Leu Val Asp Thr Gly Met Phe Arg Gly Cys Arg Ile  
 245 250 255  
 Arg Lys Glu Ile Glu Pro Phe Leu Pro Pro Leu Lys Pro Asp Tyr Cys  
 260 265 270  
 Val Lys Gln Ala Met Lys Ala Ile Leu Thr Asp Gln Pro Met Ile Cys  
 275 280 285  
 Thr Pro Arg Leu Met Tyr Ile Val Thr Phe Met Lys Ser Ile Leu Pro  
 290 295 300  
 Phe Glu Ala Val Val Cys Met Tyr Arg Phe Leu Gly Ala Asp Lys Cys  
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 325 330 335  
 Ala Lys Asn Gly Ile  
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<210> 70  
 <211> 1428  
 <212> DNA  
 <213> Homo sapiens

<400> 70

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&lt;210&gt; 71

&lt;211&gt; 289

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 71

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Met Thr Gly Val Phe Asp Arg Arg Val Pro Ser Ile Arg Ser Gly Asp
1           5           10          15
Phe Gln Ala Pro Phe Gln Thr Ser Ala Ala Met His His Pro Ser Gln
20          25          30
Glu Ser Pro Thr Leu Pro Glu Ser Ser Ala Thr Asp Ser Asp Tyr Tyr
35          40          45
Ser Pro Thr Gly Gly Ala Pro His Gly Tyr Cys Ser Pro Thr Ser Ala
50          55          60
Ser Tyr Gly Lys Ala Leu Asn Pro Tyr Gln Tyr Gln Tyr His Gly Val
65          70          75          80
Asn Gly Ser Ala Gly Ser Tyr Pro Ala Lys Ala Tyr Ala Asp Tyr Ser
85          90          95
Tyr Ala Ser Ser Tyr His Gln Tyr Gly Gly Ala Tyr Asn Arg Val Pro
100         105         110
Ser Ala Thr Asn Gln Pro Glu Lys Glu Val Thr Glu Pro Glu Val Arg
115         120         125
Met Val Asn Gly Lys Pro Lys Lys Val Arg Lys Pro Arg Thr Ile Tyr
130         135         140
Ser Ser Phe Gln Leu Ala Ala Leu Gln Arg Arg Phe Gln Lys Thr Gln
145         150         155         160
Tyr Leu Ala Leu Pro Glu Arg Ala Glu Leu Ala Ala Ser Leu Gly Leu
165         170         175
Thr Gln Thr Gln Val Lys Ile Trp Phe Gln Asn Lys Arg Ser Lys Ile
180         185         190
Lys Lys Ile Met Lys Asn Gly Glu Met Pro Pro Glu His Ser Pro Ser
195         200         205
Ser Ser Asp Pro Met Ala Cys Asn Ser Pro Gln Ser Pro Ala Val Trp

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210		215		220
Glu Pro Gln Gly Ser Ser Arg Ser Leu Ser His		His Pro His Ala His		
225		230		235
Pro Pro Thr Ser Asn Gln Ser Pro Ala Ser Ser Tyr Leu Glu Asn Ser				240
		245		250
Ala Ser Trp Tyr Thr Ser Ala Ala Ser Ser Ile Asn Ser His Leu Pro				255
		260		265
Pro Pro Gly Ser Leu Gln His Pro Leu Ala Leu Ala Ser Gly Thr Leu				270
		275		280
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Tyr				

<210> 72  
 <211> 2036  
 <212> DNA  
 <213> Homo sapiens

<400> 72  
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<210> 73  
 <211> 434  
 <212> PRT  
 <213> Homo sapiens

&lt;400&gt; 73

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 35 40 45  
 Ala Ala Gly Phe Gly Ser Val His Gln Asp Tyr Pro Ser Tyr Pro Gly  
 50 55 60  
 Phe Pro Gln Ser Gln Tyr Pro Gln Tyr Tyr Gly Ser Ser Tyr Asn Pro  
 65 70 75 80  
 Pro Tyr Val Pro Ala Ser Ser Ile Cys Pro Ser Pro Leu Ser Thr Ser  
 85 90 95  
 Thr Tyr Val Leu Gln Glu Ala Ser His Asn Val Pro Asn Gln Ser Ser  
 100 105 110  
 Glu Ser Leu Ala Gly Glu Tyr Asn Thr His Asn Gly Pro Ser Thr Pro  
 115 120 125  
 Ala Lys Glu Gly Asp Thr Asp Arg Pro His Arg Ala Ser Asp Gly Lys  
 130 135 140  
 Leu Arg Gly Arg Ser Lys Arg Ser Ser Asp Pro Ser Pro Ala Gly Asp  
 145 150 155 160  
 Asn Glu Ile Glu Arg Val Phe Val Trp Asp Leu Asp Glu Thr Ile Ile  
 165 170 175  
 Ile Phe His Ser Leu Leu Thr Gly Thr Phe Ala Ser Arg Tyr Gly Lys  
 180 185 190  
 Asp Thr Thr Thr Ser Val Arg Ile Gly Leu Met Met Glu Glu Met Ile  
 195 200 205  
 Phe Asn Leu Ala Asp Thr His Leu Phe Phe Asn Asp Leu Glu Asp Cys  
 210 215 220  
 Asp Gln Ile His Val Asp Asp Val Ser Ser Asp Asp Asn Gly Gln Asp  
 225 230 235 240  
 Leu Ser Thr Tyr Asn Phe Ser Ala Asp Gly Phe His Ser Ser Ala Pro  
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 Gly Ala Asn Leu Cys Leu Gly Ser Gly Val His Gly Gly Val Asp Trp  
 260 265 270  
 Met Arg Lys Leu Ala Phe Arg Tyr Arg Arg Val Lys Glu Met Tyr Asn  
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 Thr Tyr Lys Asn Asn Val Gly Glu Leu Ile Gly Thr Pro Lys Arg Glu  
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 325 330 335  
 Cys Val Asn Val Leu Val Thr Thr Thr Gln Leu Ile Pro Ala Leu Ala  
 340 345 350  
 Lys Val Leu Leu Tyr Gly Leu Gly Ser Val Phe Pro Ile Glu Asn Ile  
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 Tyr Ser Ala Thr Lys Thr Gly Lys Glu Ser Cys Phe Glu Arg Ile Met  
 370 375 380  
 Gln Arg Phe Gly Arg Lys Ala Val Tyr Val Val Ile Gly Asp Gly Val  
 385 390 395 400  
 Glu Glu Glu Gln Gly Ala Lys Lys His Asn Met Pro Phe Trp Arg Ile  
 405 410 415  
 Ser Cys His Ala Asp Leu Glu Ala Leu Arg His Ala Leu Glu Leu Glu  
 420 425 430  
 Tyr Leu

<210> 74  
 <211> 1907  
 <212> DNA  
 <213> Homo sapiens

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<210> 75  
 <211> 371  
 <212> PRT  
 <213> Homo sapiens

<400> 75  
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 35 40 45  
 Met Ser Leu Glu Gly Thr Glu Lys Ala Ser Trp Leu Gly Glu Gln Pro  
 50 55 60  
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 65 70 75 80  
 Glu Lys Asn Lys Tyr Asp Ala Ser Ala Ile Asp Phe Ser Arg Cys Asp

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<210> 76
<211> 3951
<212> DNA
<213> Homo sapiens
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<220>
<221> misc_feature
<222> (1)...(3951)
<223> n = A,T,C or G
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<400> 76						
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<210> 77  
 <211> 718  
 <212> PRT  
 <213> Homo sapiens

<400> 77

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Lys Ala Glu Leu Ala Asp His Gln Lys Phe Pro Cys Ser Thr Pro His
 35          40          45
Ser Ala Phe Ser Met Val Glu Glu Asp Phe Gln Gln Lys Leu Glu Ser
 50          55          60
Glu Asn Asp Leu Gln Glu Ile His Thr Ile Gln Glu Cys Lys Glu Cys
 65          70          75          80
Asp Gln Val Phe Pro Asp Leu Gln Ser Leu Glu Lys His Met Leu Ser
 85          90          95
His Thr Glu Glu Arg Glu Tyr Lys Cys Asp Gln Cys Pro Lys Ala Phe
100          105          110
Asn Trp Lys Ser Asn Leu Ile Arg His Gln Met Ser His Asp Ser Gly
115          120          125
Lys His Tyr Glu Cys Glu Asn Cys Ala Lys Val Phe Thr Asp Pro Ser
130          135          140
Asn Leu Gln Arg His Ile Arg Ser Gln His Val Gly Ala Arg Ala His
145          150          155          160
Ala Cys Pro Glu Cys Gly Lys Thr Phe Ala Thr Ser Ser Gly Leu Lys
165          170          175
Gln His Lys His Ile His Ser Ser Val Lys Pro Phe Ile Ser Phe Ser
180          185          190
Gln Ser Met Tyr Pro Phe Pro Asp Arg Asp Leu Arg Ser Leu Pro Leu
195          200          205
Lys Met Glu Pro Gln Ser Pro Gly Glu Val Lys Lys Leu Gln Lys Gly
210          215          220
Ser Ser Glu Ser Pro Phe Asp Leu Thr Thr Lys Arg Lys Asp Glu Lys
225          230          235          240
Pro Leu Thr Pro Val Pro Ser Lys Pro Pro Val Thr Pro Ala Thr Ser
245          250          255
Gln Asp Gln Pro Leu Asp Leu Ser Met Gly Ser Arg Ser Arg Ala Ser
260          265          270
Gly Thr Lys Leu Thr Glu Pro Arg Lys Asn His Val Phe Gly Gly Lys
275          280          285
Lys Gly Ser Asn Val Glu Ser Arg Pro Ala Ser Asp Gly Ser Leu Gln
290          295          300
His Ala Arg Pro Thr Pro Phe Phe Met Asp Pro Ile Tyr Arg Val Glu
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Lys Arg Lys Leu Thr Asp Pro Leu Glu Ala Leu Lys Glu Lys Tyr Leu
325          330          335
Arg Pro Ser Pro Gly Phe Leu Phe His Pro Gln Met Ser Ala Ile Glu
340          345          350
Asn Met Ala Glu Lys Leu Glu Ser Phe Ser Ala Leu Lys Pro Glu Ala
355          360          365
Ser Glu Leu Leu Gln Ser Val Pro Ser Met Phe Asn Phe Arg Ala Pro
370          375          380
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<210> 78
<211> 4950
<212> DNA
<213> Homo sapiens
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<220>  
<221> misc_feature  
<222> (1)...(4950)  
<223> n = A,T,C or G
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<210> 79

<211> 1051

<212> PRT

<213> Homo sapiens

<400> 79

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Ser Ala Phe Ser Met Val Glu Asp Phe Gln Gln Lys Leu Glu Ser
          50          55          60
Glu Asn Asp Leu Gln Glu Ile His Thr Ile Gln Glu Cys Lys Glu Cys
          65          70          75          80
Asp Gln Val Phe Pro Asp Leu Gln Ser Leu Glu Lys His Met Leu Ser
          85          90          95
His Thr Glu Glu Arg Glu Tyr Lys Cys Asp Gln Cys Pro Lys Ala Phe
          100         105         110
Asn Trp Lys Ser Asn Leu Ile Arg His Gln Met Ser His Asp Ser Gly
          115         120         125
Lys His Tyr Glu Cys Glu Asn Cys Ala Lys Val Phe Thr Asp Pro Ser
          130         135         140
Asn Leu Gln Arg His Ile Arg Ser Gln His Val Gly Ala Arg Ala His
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Ala Cys Pro Glu Cys Gly Lys Thr Phe Ala Thr Ser Ser Gly Leu Lys
          165         170         175
Gln His Lys His Ile His Ser Ser Val Lys Pro Phe Ile Cys Glu Val
          180         185         190
Cys His Lys Ser Tyr Thr Gln Phe Ser Asn Leu Cys Arg His Lys Arg
          195         200         205
Met His Ala Asp Cys Arg Thr Gln Ile Lys Cys Lys Asp Cys Gly Gln
          210         215         220
Met Phe Ser Thr Thr Ser Ser Leu Asn Lys His Arg Arg Phe Cys Glu
          225         230         235         240
Gly Lys Asn His Phe Ala Ala Gly Gly Phe Phe Gly Gln Gly Ile Ser
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Leu Pro Gly Thr Pro Ala Met Asp Lys Thr Ser Met Val Asn Met Ser
      260      265      270
His Ala Asn Pro Gly Leu Ala Asp Tyr Phe Gly Ala Asn Arg His Pro
      275      280      285
Ala Gly Leu Thr Phe Pro Thr Ala Pro Gly Phe Ser Phe Ser Val Pro
      290      295      300
Gly Leu Phe Pro Ser Gly Leu Tyr His Arg Pro Pro Leu Ile Pro Ala
305      310      315      320
Ser Ser Pro Val Lys Gly Leu Ser Ser Thr Glu Gln Thr Asn Lys Ser
      325      330      335
Gln Ser Pro Leu Met Thr His Pro Gln Ile Leu Pro Ala Thr Gln Asp
      340      345      350
Ile Leu Lys Ala Leu Ser Lys His Pro Ser Val Gly Asp Asn Lys Pro
      355      360      365
Val Glu Leu Gln Pro Glu Arg Ser Ser Glu Glu Arg Pro Phe Glu Lys
      370      375      380
Ile Ser Asp Gln Ser Glu Ser Ser Asp Leu Asp Asp Val Ser Thr Pro
385      390      395      400
Ser Gly Ser Asp Leu Glu Thr Thr Ser Gly Ser Asp Leu Glu Ser Asp
      405      410      415
Ile Glu Ser Asp Lys Glu Lys Phe Lys Glu Asn Gly Lys Met Phe Lys
      420      425      430
Asp Lys Val Ser Pro Leu Gln Asn Leu Ala Ser Ile Asn Asn Lys Lys
      435      440      445
Glu Tyr Ser Asn His Ser Ile Phe Ser Pro Ser Leu Glu Glu Gln Thr
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Ala Val Ser Gly Ala Val Asn Asp Ser Ile Lys Ala Ile Ala Ser Ile
465      470      475      480
Ala Glu Lys Tyr Phe Gly Ser Thr Gly Leu Val Gly Leu Gln Asp Lys
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Lys Val Gly Ala Leu Pro Tyr Pro Ser Met Phe Pro Leu Pro Phe Phe
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Pro Ala Phe Ser Gln Ser Met Tyr Pro Phe Pro Asp Arg Asp Leu Arg
      515      520      525
Ser Leu Pro Leu Lys Met Glu Pro Gln Ser Pro Gly Glu Val Lys Lys
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Leu Gln Lys Gly Ser Ser Glu Ser Pro Phe Asp Leu Thr Thr Lys Arg
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Lys Asp Glu Lys Pro Leu Thr Pro Val Pro Ser Lys Pro Pro Val Thr
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Pro Ala Thr Ser Gln Asp Gln Pro Leu Asp Leu Ser Met Gly Ser Arg
      580      585      590
Ser Arg Ala Ser Gly Thr Lys Leu Thr Glu Pro Arg Lys Asn His Val
      595      600      605
Phe Gly Gly Lys Lys Gly Ser Asn Val Glu Ser Arg Pro Ala Ser Asp
610      615      620
Gly Ser Leu Gln His Ala Arg Pro Thr Pro Phe Phe Met Asp Pro Ile
625      630      635      640
Tyr Arg Val Glu Lys Arg Lys Leu Thr Asp Pro Leu Glu Ala Leu Lys
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Glu Lys Tyr Leu Arg Pro Ser Pro Gly Phe Leu Phe His Pro Gln Phe
      660      665      670
Gln Leu Pro Asp Gln Arg Thr Trp Met Ser Ala Ile Glu Asn Met Ala
675      680      685
Glu Lys Leu Glu Ser Phe Ser Ala Leu Lys Pro Glu Ala Ser Glu Leu
690      695      700
Leu Gln Ser Val Pro Ser Met Phe Asn Phe Arg Ala Pro Pro Asn Ala
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Leu Pro Glu Asn Leu Leu Arg Lys Gly Lys Glu Arg Tyr Thr Cys Arg
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Tyr Cys Gly Lys Ile Phe Pro Arg Ser Ala Asn Leu Thr Arg His Leu
      740      745      750
Arg Thr His Thr Gly Glu Gln Pro Tyr Arg Cys Lys Tyr Cys Asp Arg
      755      760      765
Ser Phe Ser Ile Ser Ser Asn Leu Gln Arg His Val Arg Asn Ile His
      770      775      780
Asn Lys Glu Lys Pro Phe Lys Cys His Leu Cys Tyr Arg Cys Phe Gly
785      790      795      800
Gln Gln Thr Asn Leu Asp Arg His Leu Lys Lys His Glu Asn Gly Asn
      805      810      815
Met Ser Gly Thr Ala Thr Ser Ser Pro His Ser Glu Leu Glu Ser Thr
      820      825      830
Gly Ala Ile Leu Asp Asp Lys Glu Asp Ala Tyr Phe Thr Glu Ile Arg
      835      840      845
Asn Phe Ile Gly Asn Ser Asn His Gly Ser Gln Ser Pro Arg Asn Val
      850      855      860
Glu Glu Arg Met Asn Gly Ser His Phe Lys Glu Glu Lys Ala Leu Val
865      870      875      880
Pro Ser Gln Asn Ser Asp Leu Leu Asp Asp Glu Glu Val Glu Asp Glu
      885      890      895
Val Leu Leu Asp Glu Glu Asp Glu Asp Tyr Asp Ile Thr Gly Lys Thr
      900      905      910
Gly Lys Glu Glu Thr Ser Asn Leu His Glu Gly Asn Pro Glu Asp
      915      920      925
Asp Tyr Glu Glu Thr Ser Ala Leu Glu Met Ser Cys Lys Thr Ser Pro
      930      935      940
Val Arg Tyr Lys Glu Glu Glu Tyr Lys Ser Gly Leu Ser Ala Leu Asp
945      950      955      960
His Ile Arg His Phe Thr Asp Ser Leu Lys Met Arg Lys Met Glu Asp
      965      970      975
Asn Gln Tyr Ser Glu Ala Glu Leu Ser Ser Phe Ser Thr Ser His Val
      980      985      990
Pro Glu Glu Leu Lys Gln Pro Leu His Arg Lys Ser Lys Ser Gln Ala
      995      1000      1005
Tyr Ala Met Met Leu Ser Leu Ser Asp Lys Glu Ser Leu His Ser Thr
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Ser His Ser Ser Ser Asn Val Trp His Ser Met Ala Arg Ala Ala Ala
1025      1030      1035      1040
Glu Ser Ser Ala Ile Gln Ser Ile Ser His Val
      1045      1050

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&lt;210&gt; 80

&lt;211&gt; 3978

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(3978)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 80

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<211> 727

<212> PRT

<213> Homo sapiens

<400> 81

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Lys	Ala	Glu	Leu	Ala	Asp	His	Gln	Lys	Phe	Pro	Cys	Ser	Thr	Pro	His
		35					40					45			
Ser	Ala	Phe	Ser	Met	Val	Glu	Glu	Asp	Phe	Gln	Gln	Lys	Leu	Glu	Ser
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Glu	Asn	Asp	Leu	Gln	Glu	Ile	His	Thr	Ile	Gln	Glu	Cys	Lys	Glu	Cys
65				70					75					80	
Asp	Gln	Val	Phe	Leu	Asp	Leu	Gln	Ser	Leu	Glu	Lys	His	Met	Leu	Ser
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His	Thr	Glu	Glu	Arg	Glu	Tyr	Lys	Cys	Asp	Gln	Cys	Pro	Lys	Ala	Phe
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Asn	Trp	Lys	Ser	Asn	Leu	Ile	Arg	His	Gln	Met	Ser	His	Asp	Ser	Gly
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Asn	Leu	Gln	Arg	His	Ile	Arg	Ser	Gln	His	Val	Gly	Ala	Arg	Ala	His
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Pro Phe Lys Cys His Leu Cys Tyr Arg Cys Phe Gly Gln Gln Thr Asn
465              470              475              480
Leu Asp Arg His Leu Lys Lys His Glu Asn Gly Asn Met Ser Gly Thr
      485              490              495
Ala Thr Ser Ser Pro His Ser Glu Leu Glu Ser Thr Gly Ala Ile Leu
      500              505              510
Asp Asp Lys Glu Asp Ala Tyr Phe Thr Glu Ile Arg Asn Phe Ile Gly
      515              520              525
Asn Ser Asn His Gly Ser Gln Ser Pro Arg Asn Val Glu Glu Arg Met
      530              535              540
Asn Gly Ser His Phe Lys Glu Glu Lys Ala Leu Val Pro Ser Gln Asn
545              550              555              560
Ser Asp Leu Leu Asp Asp Glu Glu Val Glu Asp Glu Val Leu Leu Asp
      565              570              575
Glu Glu Asp Glu Asp Tyr Asp Ile Thr Gly Lys Thr Gly Lys Glu Pro
      580              585              590
Val Thr Ser Asn Leu His Glu Gly Asn Pro Glu Asp Asp Tyr Glu Glu
      595              600              605
Thr Ser Ala Leu Glu Met Ser Cys Lys Thr Ser Pro Val Arg Tyr Lys
      610              615              620
Glu Glu Glu Tyr Lys Ser Gly Leu Ser Ala Leu Asp His Ile Arg His
625              630              635              640
Phe Thr Asp Ser Leu Lys Met Arg Lys Met Glu Asp Asn Gln Tyr Ser
      645              650              655
Glu Ala Glu Leu Ser Ser Phe Ser Thr Ser His Val Pro Glu Glu Leu
      660              665              670
Lys Gln Pro Leu His Arg Lys Ser Lys Ser Gln Ala Tyr Ala Met Met
      675              680              685
Leu Ser Leu Ser Asp Lys Glu Ser Leu His Ser Thr Ser His Ser Ser
      690              695              700
Ser Asn Val Trp His Ser Met Ala Arg Ala Ala Glu Ser Ser Ala
705              710              715              720
Ile Gln Ser Ile Ser His Val
      725

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&lt;210&gt; 82

&lt;211&gt; 4923

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(4923)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 82

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&lt;210&gt; 83

&lt;211&gt; 1042

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 83

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Glu Glu Arg Gln Tyr Arg Cys Glu Asp Cys Asp Gln Leu Phe Glu Ser
      20           25           30
Lys Ala Glu Leu Ala Asp His Gln Lys Phe Pro Cys Ser Thr Pro His
      35           40           45
Ser Ala Phe Ser Met Val Glu Glu Asp Phe Gln Gln Lys Leu Glu Ser
      50           55           60
Glu Asn Asp Leu Gln Glu Ile His Thr Ile Gln Glu Cys Lys Glu Cys
      65           70           75           80
Asp Gln Val Phe Pro Asp Leu Gln Ser Leu Glu Lys His Met Leu Ser
      85           90           95
His Thr Glu Glu Arg Glu Tyr Lys Cys Asp Gln Cys Pro Lys Ala Phe
      100          105          110
Asn Trp Lys Ser Asn Leu Ile Arg His Gln Met Ser His Asp Ser Gly
      115          120          125
Lys His Tyr Glu Cys Glu Asn Cys Ala Lys Val Phe Thr Asp Pro Ser
      130          135          140
Asn Leu Gln Arg His Ile Arg Ser Gln His Val Gly Ala Arg Ala His
      145          150          155          160
Ala Cys Pro Glu Cys Gly Lys Thr Phe Ala Thr Ser Ser Gly Leu Lys
      165          170          175
Gln His Lys His Ile His Ser Ser Val Lys Pro Phe Ile Cys Glu Val
      180          185          190

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Cys	His	Lys	Ser	Tyr	Thr	Gln	Phe	Ser	Asn	Leu	Cys	Arg	His	Lys	Arg	195	200	205
Met	His	Ala	Asp	Cys	Arg	Thr	Gln	Ile	Lys	Cys	Lys	Asp	Cys	Gly	Gln	210	215	220
Met	Phe	Ser	Thr	Thr	Ser	Ser	Leu	Asn	Lys	His	Arg	Arg	Phe	Cys	Glu	225	230	235
Gly	Lys	Asn	His	Phe	Ala	Ala	Gly	Gly	Phe	Phe	Gly	Gln	Gly	Ile	Ser	245	250	255
Leu	Pro	Gly	Thr	Pro	Ala	Met	Asp	Lys	Thr	Ser	Met	Val	Asn	Met	Ser	260	265	270
His	Ala	Asn	Pro	Gly	Leu	Ala	Asp	Tyr	Phe	Gly	Ala	Asn	Arg	His	Pro	275	280	285
Ala	Gly	Leu	Thr	Phe	Pro	Thr	Ala	Pro	Gly	Phe	Ser	Phe	Ser	Phe	Pro	290	295	300
Gly	Leu	Phe	Pro	Ser	Gly	Leu	Tyr	His	Arg	Pro	Pro	Leu	Ile	Pro	Ala	305	310	315
Ser	Ser	Pro	Val	Lys	Gly	Leu	Ser	Ser	Thr	Glu	Gln	Thr	Asn	Lys	Ser	325	330	335
Gln	Ser	Pro	Leu	Met	Thr	His	Pro	Gln	Ile	Leu	Pro	Ala	Thr	Gln	Asp	340	345	350
Ile	Leu	Lys	Ala	Leu	Ser	Lys	His	Pro	Ser	Val	Gly	Asp	Asn	Lys	Pro	355	360	365
Val	Glu	Leu	Gln	Pro	Glu	Arg	Ser	Ser	Glu	Glu	Arg	Pro	Phe	Glu	Lys	370	375	380
Ile	Ser	Asp	Gln	Ser	Glu	Ser	Ser	Asp	Leu	Asp	Asp	Val	Ser	Thr	Pro	385	390	395
Ser	Gly	Ser	Asp	Leu	Glu	Thr	Thr	Ser	Gly	Ser	Asp	Leu	Glu	Ser	Asp	405	410	415
Ile	Glu	Ser	Asp	Lys	Glu	Lys	Phe	Lys	Glu	Asn	Gly	Lys	Met	Phe	Lys	420	425	430
Asp	Lys	Val	Ser	Pro	Leu	Gln	Asn	Leu	Ala	Ser	Ile	Asn	Asn	Lys	Lys	435	440	445
Glu	Tyr	Ser	Asn	His	Ser	Ile	Phe	Ser	Pro	Ser	Leu	Glu	Glu	Gln	Thr	450	455	460
Ala	Val	Ser	Gly	Ala	Val	Asn	Asp	Ser	Ile	Lys	Ala	Ile	Ala	Ser	Ile	465	470	475
Ala	Glu	Lys	Tyr	Phe	Gly	Ser	Thr	Gly	Leu	Val	Gly	Leu	Gln	Asp	Lys	485	490	495
Lys	Val	Gly	Ala	Leu	Pro	Tyr	Pro	Ser	Met	Phe	Pro	Leu	Pro	Phe	Phe	500	505	510
Pro	Ala	Phe	Ser	Gln	Ser	Met	Tyr	Pro	Phe	Pro	Asp	Arg	Asp	Leu	Arg	515	520	525
Ser	Leu	Pro	Leu	Lys	Met	Glu	Pro	Gln	Ser	Pro	Gly	Glu	Val	Lys	Lys	530	535	540
Leu	Gln	Lys	Gly	Ser	Ser	Glu	Ser	Pro	Phe	Asp	Leu	Thr	Thr	Lys	Arg	545	550	555
Lys	Asp	Glu	Lys	Pro	Leu	Thr	Pro	Val	Pro	Ser	Lys	Pro	Pro	Val	Thr	565	570	575
Pro	Ala	Thr	Ser	Gln	Asp	Gln	Pro	Leu	Asp	Leu	Ser	Met	Gly	Ser	Arg	580	585	590
Ser	Arg	Ala	Ser	Gly	Thr	Lys	Leu	Thr	Glu	Pro	Arg	Lys	Asn	His	Val	595	600	605
Phe	Gly	Gly	Lys	Lys	Gly	Ser	Asn	Val	Glu	Ser	Arg	Pro	Ala	Ser	Asp	610	615	620
Gly	Ser	Leu	Gln	His	Ala	Arg	Pro	Thr	Pro	Phe	Phe	Met	Asp	Pro	Ile	625	630	635
Tyr	Arg	Val	Glu	Lys	Arg	Lys	Leu	Thr	Asp	Pro	Leu	Glu	Ala	Leu	Lys	645	650	655

Glu Lys Tyr Leu Arg Pro Ser Pro Gly Phe Leu Phe His Pro Gln Met  
 660 665 670  
 Ser Ala Ile Glu Asn Met Ala Glu Lys Leu Glu Ser Phe Ser Ala Leu  
 675 680 685  
 Lys Pro Glu Ala Ser Glu Leu Leu Gln Ser Val Pro Ser Met Phe Asn  
 690 695 700  
 Phe Arg Ala Pro Pro Asn Ala Leu Pro Glu Asn Leu Leu Arg Lys Gly  
 705 710 715 720  
 Lys Glu Arg Tyr Thr Cys Arg Tyr Cys Gly Lys Ile Phe Pro Arg Ser  
 725 730 735  
 Ala Asn Leu Thr Arg His Leu Arg Thr His Thr Gly Glu Gln Pro Tyr  
 740 745 750  
 Arg Cys Lys Tyr Cys Asp Arg Ser Phe Ser Ile Ser Ser Asn Leu Gln  
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 Arg His Val Arg Asn Ile His Asn Lys Glu Lys Pro Phe Lys Cys His  
 770 775 780  
 Leu Cys Asp Arg Cys Phe Gly Gln Gln Thr Asn Leu Asp Arg His Leu  
 785 790 795 800  
 Lys Lys His Glu Asn Gly Asn Met Ser Gly Thr Ala Thr Ser Ser Pro  
 805 810 815  
 His Ser Glu Leu Glu Ser Thr Gly Ala Ile Leu Asp Asp Lys Glu Asp  
 820 825 830  
 Ala Tyr Phe Thr Glu Ile Arg Asn Phe Ile Gly Asn Ser Asn His Gly  
 835 840 845  
 Ser Gln Ser Pro Arg Asn Val Glu Glu Arg Met Asn Gly Ser His Phe  
 850 855 860  
 Lys Asp Glu Lys Ala Leu Val Thr Ser Gln Asn Ser Asp Leu Leu Asp  
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 Asp Glu Glu Val Glu Asp Glu Val Leu Leu Asp Glu Glu Asp Glu Asp  
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 Asn Asp Ile Thr Gly Lys Thr Gly Lys Glu Pro Val Thr Ser Asn Leu  
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 His Glu Gly Asn Pro Glu Asp Asp Tyr Glu Glu Thr Ser Ala Leu Glu  
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 Ser Phe Ser Thr Ser His Val Pro Glu Glu Leu Lys Gln Pro Leu His  
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 Arg Lys Ser Lys Ser Gln Ala Tyr Ala Met Met Leu Ser Leu Ser Asp  
 995 1000 1005  
 Lys Glu Ser Leu His Ser Thr Ser His Ser Ser Ser Asn Val Trp His  
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 1025 1030 1035 1040  
 His Val

&lt;210&gt; 84

&lt;211&gt; 4039

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 84

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101

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ttatgtaata ttgccaatga tgaattcagg ttgttttttag cacaagtttc tcttttttat 3960
gctggtattc tcaactgccac atttttggaa acctgtatta caccttaaat ctatcaataa 4020
atgatagttt tctaattct                                     4039

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&lt;210&gt; 85

&lt;211&gt; 595

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 85

```

Val Gly Ser Gly Ile Ser Phe Gln Pro Gly Ala Ile Gly Val Glu Val
1      5      10      15
Ser Ala Met Asn Pro Val Asn Ala Thr Ala Leu Tyr Ile Ser Ala Ser
20     25     30
Arg Leu Val Leu Asn Tyr Asp Pro Gly Asp Pro Lys Ala Phe Thr Glu
35     40     45
Ile Asn Arg Leu Leu Pro Tyr Phe Arg Gln Ser Leu Ser Cys Cys Val
50     55     60
Cys Gly His Leu Leu Gln Asp Pro Ile Ala Pro Thr Asn Ser Thr Cys
65     70     75     80
Gln His Tyr Val Cys Lys Thr Cys Lys Gly Lys Lys Met Met Met Lys
85     90     95
Pro Ser Cys Ser Trp Cys Lys Asp Tyr Glu Gln Phe Glu Glu Asn Lys
100    105    110
Gln Leu Ser Ile Leu Val Asn Cys Tyr Lys Lys Leu Cys Glu Tyr Ile
115    120    125
Thr Gln Thr Thr Leu Ala Arg Asp Ile Ile Glu Ala Val Asp Cys Ser
130    135    140
Ser Asp Ile Leu Ala Leu Leu Asn Asp Gly Ser Leu Phe Cys Glu Glu
145    150    155    160
Thr Glu Lys Pro Ser Asp Ser Ser Phe Thr Leu Cys Leu Thr His Ser
165    170    175
Pro Leu Pro Ser Thr Ser Glu Pro Thr Thr Asp Pro Gln Ala Ser Leu
180    185    190
Ser Pro Met Ser Glu Ser Thr Leu Ser Ile Ala Ile Gly Ser Ser Val
195    200    205
Ile Asn Gly Leu Pro Thr Tyr Asn Gly Leu Ser Ile Asp Arg Phe Gly
210    215    220
Ile Asn Ile Pro Ser Pro Glu His Ser Asn Thr Ile Asp Val Cys Asn
225    230    235    240
Thr Val Asp Ile Lys Thr Glu Asp Leu Ser Asp Ser Leu Pro Pro Val
245    250    255
Cys Asp Thr Val Ala Thr Asp Leu Cys Ser Thr Gly Ile Asp Ile Cys
260    265    270
Ser Phe Ser Glu Asp Ile Lys Pro Gly Asp Ser Leu Leu Leu Ser Val
275    280    285
Glu Glu Val Leu Arg Ser Leu Glu Thr Val Ser Asn Thr Glu Val Cys
290    295    300
Cys Pro Asn Leu Gln Pro Asn Leu Glu Ala Thr Val Ser Asn Gly Pro
305    310    315    320
Phe Leu Gln Leu Ser Ser Gln Ser Leu Ser His Asn Val Phe Met Ser

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<210> 86
<211> 1385
<212> DNA
<213> Homo sapiens
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<400> 86						
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atcattcaga	agagaaggcc	tcaaatgtac	tggaagaaat	tgccaaggac	aaagttttaa	180
aagactttta	tgttcataca	gtaatgactt	gttatttttag	tttatttgga	atagacaata	240
tggctcttag	tccctggctcat	atattgagag	tttacgggtg	tgttttgcct	tggtctgttg	300
ctttggactg	gctcacagaa	aagccagaac	tgttccaact	agcactgaaa	gcattcaggt	360
atactctgaa	actaatgatt	gataaagcaa	gtttagggtcc	aatagaagac	tttagaagac	420
tgattaagta	ccttgaagaa	tatgaacgtg	actggtacat	tggtttggta	tctgatgaaa	480
agtggaagga	agcaatttta	caagaaaagc	catacttggt	ttctctgggg	tatgattcta	540
atatgggaat	ttacactggg	agagtgttta	gccttcaaga	attatgtatc	caagtgggaa	600
agttaaatcc	tgaagctggt	agaggtcagt	gggccaatct	ttcatgggaa	ttactttatg	660
ccacaaacga	tgatgaagaa	cgttatagta	tacaagctca	tccactactt	ttaagaaatc	720
ttacggcata	agcagcagaa	cctccccctgg	gatatccgat	ttaattctta	aaacctctcc	780
acatacatatt	gtattagagc	tcaatttgac	tgtaatgtca	tcaaatgcaa	tgttttttatt	840
ttttcatcct	aaaaaagtaa	ctgtgattct	tgtaacttga	ggacttctcc	acaccccat	900

103

```

tcagatgcct gagaacagct aagctccgta aagttgggtc tcttagccat cttaatgggt 960
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ttttc 1385

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&lt;210&gt; 87

&lt;211&gt; 252

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 87

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Met Pro Ser Ser Lys Met Lys Glu Met Ser Ser Leu Phe Pro Glu Asp
1      5      10      15
Trp Tyr Gln Phe Val Leu Arg Gln Leu Glu Cys Tyr His Ser Glu Glu
20      25      30
Lys Ala Ser Asn Val Leu Glu Glu Ile Ala Lys Asp Lys Val Leu Lys
35      40      45
Asp Phe Tyr Val His Thr Val Met Thr Cys Tyr Phe Ser Leu Phe Gly
50      55      60
Ile Asp Asn Met Ala Pro Ser Pro Gly His Ile Leu Arg Val Tyr Gly
65      70      75      80
Gly Val Leu Pro Trp Ser Val Ala Leu Asp Trp Leu Thr Glu Lys Pro
85      90      95
Glu Leu Phe Gln Leu Ala Leu Lys Ala Phe Arg Tyr Thr Leu Lys Leu
100     105     110
Met Ile Asp Lys Ala Ser Leu Gly Pro Ile Glu Asp Phe Arg Glu Leu
115     120     125
Ile Lys Tyr Leu Glu Glu Tyr Glu Arg Asp Trp Tyr Ile Gly Leu Val
130     135     140
Ser Asp Glu Lys Trp Lys Glu Ala Ile Leu Gln Glu Lys Pro Tyr Leu
145     150     155     160
Phe Ser Leu Gly Tyr Asp Ser Asn Met Gly Ile Tyr Thr Gly Arg Val
165     170     175
Leu Ser Leu Gln Glu Leu Leu Ile Gln Val Gly Lys Leu Asn Pro Glu
180     185     190
Ala Val Arg Gly Gln Trp Ala Asn Leu Ser Trp Glu Leu Leu Tyr Ala
195     200     205
Thr Asn Asp Asp Glu Glu Arg Tyr Ser Ile Gln Ala His Pro Leu Leu
210     215     220
Leu Arg Asn Leu Thr Val Gln Ala Ala Glu Pro Pro Leu Gly Tyr Pro
225     230     235     240
Ile Tyr Ser Ser Lys Pro Leu His Ile His Leu Tyr
245     250

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&lt;210&gt; 88

&lt;211&gt; 4660

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 88

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ttgatcgacc aggaaaatac gagggcggag ggaccatggt cacctacaag cgtccaaatg 120

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ggaccaacgc	catcagcccc	caggtgccac	cccacaggag	accaggggaa	cccttcaatg	300
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tcccagtcag	gcatccagac	agattttctc	cccacgacc	ggacaacttg	gtgccaccag	480
caccgcagcc	cccacggcgc	agccgggac	acaactggaa	gcagcttggg	acaacagaat	540
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&lt;210&gt; 89

&lt;211&gt; 538

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 89

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Met Phe Thr Tyr Lys Arg Pro Asn Glu Ile Ser Ser Thr Ala Gly Glu
 1          5          10          15
Ser Phe Leu Ala Glu Gly Pro Thr Asn Glu Ile Leu Asp Val Tyr Met
          20          25          30
Ile His Gln Gln Pro Asn Pro Gly Val His Tyr Glu Tyr Val Ile Met
          35          40          45
Gly Thr Asn Ala Ile Ser Pro Gln Val Pro Pro His Arg Arg Pro Gly
          50          55          60
Glu Pro Phe Asn Gly Gln Met Val Thr Glu Gly Arg Ser Gln Glu Glu
65          70          75          80
Gly Glu Gln Lys Gly Arg Asn Glu Glu Lys Glu Asp Leu Arg Gly Glu
          85          90          95
Ala Pro Glu Met Phe Thr Ser Glu Ser Ala Gln Thr Phe Pro Val Arg
          100          105          110
His Pro Asp Arg Phe Ser Pro His Arg Pro Asp Asn Leu Val Pro Pro
          115          120          125
Ala Pro Gln Pro Pro Arg Arg Ser Arg Asp His Asn Trp Lys Gln Leu
          130          135          140
Gly Thr Thr Glu Cys Ser Thr Thr Cys Gly Lys Gly Ser Gln Tyr Pro
145          150          155          160
Ile Phe Arg Cys Val His Arg Ser Thr His Glu Glu Ala Pro Glu Ser
          165          170          175
Tyr Cys Asp Ser Ser Met Lys Pro Thr Pro Glu Glu Glu Pro Cys Asn
          180          185          190
Ile Phe Pro Cys Pro Ala Phe Trp Asp Ile Gly Glu Trp Ser Glu Cys
          195          200          205
Ser Lys Thr Cys Gly Leu Gly Met Gln His Arg Gln Val Leu Cys Arg
          210          215          220
Gln Val Tyr Ala Asn Arg Ser Leu Thr Val Gln Pro Tyr Arg Cys Gln
225          230          235          240
His Leu Glu Lys Pro Glu Thr Thr Ser Thr Cys Gln Leu Lys Ile Cys
          245          250          255
Ser Glu Trp Gln Ile Arg Thr Asp Trp Thr Ser Cys Ser Val Pro Cys

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106

	260		265		270
Gly Val	Gly Gln Arg Thr Arg Asp	Val Lys Cys	Val Ser Asn Ile Gly		
	275	280	285		
Asp Val	Val Asp Asp Glu Glu Cys	Asn Met Lys	Leu Arg Pro Asn Asp		
	290	295	300		
Ile Glu	Asn Cys Asp Met Gly Pro	Cys Ala Lys	Ser Trp Phe Leu Thr		
	305	310	315		320
Glu Trp	Ser Glu Arg Ser Ser Ala	Glu Cys Gly	Ala Gly Val Arg Thr		
	325	330	335		
Arg Ser	Val Val Cys Met Thr Asn	His Val Ser	Ser Leu Pro Leu Glu		
	340	345	350		
Gly Cys	Gly Asn Asn Arg Pro Ala	Glu Ala Thr	Pro Cys Asp Asn Gly		
	355	360	365		
Pro Cys	Thr Gly Lys Val Glu Trp	Phe Ala Gly	Ser Trp Ser Gln Cys		
	370	375	380		
Ser Ile	Glu Cys Gly Ser Gly Thr	Gln Gln Arg	Glu Val Ile Cys Val		
	385	390	395		400
Arg Lys	Asn Ala Asp Thr Phe Glu	Val Leu Asp	Pro Ser Glu Cys Ser		
	405	410	415		
Phe Leu	Glu Lys Pro Pro Ser Gln	Gln Ser Cys	His Leu Lys Pro Cys		
	420	425	430		
Gly Ala	Lys Trp Phe Ser Thr Glu	Trp Ser Met	Cys Ser Lys Ser Cys		
	435	440	445		
Gln Gly	Gly Phe Arg Val Arg Glu	Val Arg Cys	Leu Ser Asp Asp Met		
	450	455	460		
Thr Leu	Ser Asn Leu Cys Asp Pro	Gln Leu Lys	Pro Glu Glu Arg Glu		
	465	470	475		480
Ser Cys	Asn Pro Gln Asp Cys Val	Pro Glu Val	Asp Glu Asn Cys Lys		
	485	490	495		
Asp Lys	Tyr Tyr Asn Cys Asn Val	Val Val Gln	Ala Arg Leu Cys Val		
	500	505	510		
Tyr Asn	Tyr Tyr Lys Thr Ala Cys	Cys Ala Ser	Cys Thr Arg Val Ala		
	515	520	525		
Asn Arg	Gln Thr Gly Phe Leu Gly	Ser Arg			
	530	535			

&lt;210&gt; 90

&lt;211&gt; 4793

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 90

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ccctcaggaa  ggtgccttag  gcctgttga  ttctatttta  ttgccacct  tttcctggag  2160
cccaggtcca  ggcccggcag  gactctgcag  gtcactgcta  gctccagatg  agaccgtcca  2220
gcgttcccc  ttcaagagaa  aactcatcc  cgaacagcct  aaaaaattcc  catcccttct  2280
ttctacccc  tccatatcta  tatctccga  gtggctggac  aaaatgagct  acgtctgggt  2340
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tcctcataca tctccaaatt gtttaaactt actttatgag tgtttgttta gaagttcgga 4560
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tccctgcccc gaaacttagg aagcatgaaa taaatcaaatt gtttattttt cttcttattt 4680
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cttaaagaca agcaaggagg attgatatat gtacaatttg ctctcatgtt ttt 4793

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&lt;210&gt; 91

&lt;211&gt; 625

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 91

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Met Ser Gln Glu Ser Asp Asn Asn Lys Arg Leu Val Ala Leu Val Pro
 1          5          10          15
Met Pro Ser Asp Pro Pro Phe Asn Thr Arg Arg Ala Tyr Thr Ser Glu
          20          25          30
Asp Glu Ala Trp Lys Ser Tyr Leu Glu Asn Pro Leu Thr Ala Ala Thr
          35          40          45
Lys Ala Met Met Ile Ile Asn Gly Asp Glu Asp Ser Ala Ala Ala Leu
          50          55          60
Gly Leu Leu Tyr Asp Tyr Tyr Lys Val Pro Arg Asp Lys Arg Leu Leu
65          70          75          80
Ser Val Ser Lys Ala Ser Asp Ser Gln Glu Asp Gln Glu Lys Arg Asn
          85          90          95
Cys Leu Gly Thr Ser Glu Ala Gln Ser Asn Leu Ser Gly Gly Glu Asn
          100          105          110
Arg Val Gln Val Leu Lys Thr Val Pro Val Asn Leu Ser Leu Asn Gln
          115          120          125
Asp His Leu Glu Asn Ser Lys Arg Glu Gln Tyr Ser Ile Ser Phe Pro
130          135          140
Glu Ser Ser Ala Ile Ile Pro Val Ser Gly Ile Thr Val Val Lys Ala
145          150          155          160
Glu Asp Phe Thr Pro Val Phe Met Ala Pro Pro Val His Tyr Pro Arg
          165          170          175
Gly Asp Gly Glu Glu Gln Arg Val Val Ile Phe Glu Gln Thr Gln Tyr
          180          185          190
Asp Val Pro Ser Leu Ala Thr His Ser Ala Tyr Leu Lys Asp Asp Gln
          195          200          205
Arg Ser Thr Pro Asp Ser Thr Tyr Ser Glu Ser Phe Lys Asp Ala Ala
210          215          220
Thr Glu Lys Phe Arg Ser Ala Ser Val Gly Ala Glu Glu Tyr Met Tyr
225          230          235          240
Asp Gln Thr Ser Ser Gly Thr Phe Gln Tyr Thr Leu Glu Ala Thr Lys
          245          250          255
Ser Leu Arg Gln Lys Gln Gly Glu Gly Pro Met Thr Tyr Leu Asn Lys
          260          265          270
Gly Gln Phe Tyr Ala Ile Thr Leu Ser Glu Thr Gly Asp Asn Lys Cys
          275          280          285
Phe Arg His Pro Ile Ser Lys Val Arg Ser Val Val Met Val Val Phe
290          295          300
Ser Glu Asp Lys Asn Arg Asp Glu Gln Leu Lys Tyr Trp Lys Tyr Trp
305          310          315          320
His Ser Arg Gln His Thr Ala Lys Gln Arg Val Leu Asp Ile Ala Asp
          325          330          335
Tyr Lys Glu Ser Phe Asn Thr Ile Gly Asn Ile Glu Glu Ile Ala Tyr
          340          345          350

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Asn Ala Val Ser Phe Thr Trp Asp Val Asn Glu Glu Ala Lys Ile Phe  
           355                          360                          365  
 Ile Thr Val Asn Cys Leu Ser Thr Asp Phe Ser Ser Gln Lys Gly Val  
           370                          375                          380  
 Lys Gly Leu Pro Leu Met Ile Gln Ile Asp Thr Tyr Ser Tyr Asn Asn  
           385                          390                          395                          400  
 Arg Ser Asn Lys Pro Ile His Arg Ala Tyr Cys Gln Ile Lys Val Phe  
                           405                          410                          415  
 Cys Asp Lys Gly Ala Glu Arg Lys Ile Arg Asp Glu Glu Gln Lys Gln  
                           420                          425                          430  
 Asn Arg Lys Asn Gly Lys Gly Gln Ala Ser Gln Thr Gln Cys Asn Ser  
           435                          440                          445  
 Ser Ser Asp Gly Lys Leu Ala Ile Pro Leu Gln Lys Lys Ser Asp  
           450                          455                          460  
 Ile Thr Tyr Phe Lys Thr Met Pro Asp Leu His Ser Gln Pro Val Leu  
           465                          470                          475                          480  
 Phe Ile Pro Asp Val His Phe Ala Asn Leu Gln Arg Thr Gly Gln Val  
                           485                          490                          495  
 Tyr Tyr Asn Thr Asp Asp Glu Arg Glu Gly Gly Ser Val Leu Val Lys  
                           500                          505                          510  
 Arg Met Phe Arg Pro Met Glu Glu Glu Phe Gly Pro Val Pro Ser Lys  
           515                          520                          525  
 Gln Met Lys Glu Glu Gly Thr Lys Arg Val Leu Leu Tyr Val Arg Lys  
           530                          535                          540  
 Glu Thr Asp Asp Val Phe Asp Ala Leu Met Leu Lys Ser Pro Thr Val  
           545                          550                          555                          560  
 Met Gly Leu Met Glu Ala Ile Ser Glu Lys Tyr Gly Leu Pro Val Glu  
                           565                          570                          575  
 Lys Ile Ala Lys Leu Tyr Lys Lys Ser Lys Lys Gly Ile Leu Val Asn  
                           580                          585                          590  
 Met Asp Asp Asn Ile Ile Glu His Tyr Ser Asn Glu Asp Thr Phe Ile  
           595                          600                          605  
 Leu Asn Met Glu Ser Met Val Glu Gly Phe Lys Val Thr Leu Met Glu  
           610                          615                          620  
 Ile  
 625

&lt;210&gt; 92

&lt;211&gt; 2085

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 92

ggctgcagtt acagagtgtt gccatcacca agtatgtggc ggacgtcctg ccggggaaga 60  
 atcaaagagc agagagcatg gccagtgcag cgagggaact gggttatccag cgggttgagtc 120  
 tggtagaggag tctttgcgag agcgaggagc agcgggtact ggaacaggtg catggcgaag 180  
 aggagcgggc ccaccagagc atcctgacac agcgggtgca ctgggccgag gcgctgcaga 240  
 aacttgacac catccgcact ggcctggtgg gcatgcttac tcacctggat gacctccagc 300  
 tgattcagaa ggagcaagag attttcgaga ggaccgaaga agcagagggc attttggatc 360  
 cccaggagtc ggaaatgtta aactttaatg agaagtgcac tcggagccca ctactgacct 420  
 aactctgggc aacggcggtt cttgggtctc tctcaggcac agaggacata cggatcgatg 480  
 agaggacagt cagccccctt ctgcaattgt cagatgatcg aaagaccctg accttcagca 540  
 ccaagaagtc aaaggcctgt gcagatggcc cggagcgctt cgaccactgg cccaatgccc 600  
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 gtgcctataa ggtggcggtg gcttcaggcc acctgccccg caagggttct ggcatgtact 720  
 gccgtctggg ccacaatgcc ttctcctggg tcttctctcg ctatgatcag gagtttcggt 780  
 tctcacacaa tgggcagcac gagcccctgg ggctgctgcg gggcccagcc cagctggggtg 840

110

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tagtgctgga cttgcaggtt caggagctgc tcttctatga gccagcctcc ggcatagtgc 900
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agaccatttc tatcgctccg tgacctctgg ccacaggaag ccagggtccac cgccccaccac 1020
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gatggcttaa agccagaaag agctgaggga gttaagaggg ccaaccttag ggcacgtggg 2040
cattatataa ggtcttaaaa gcattaaaaa aaaaaaaaaa aaaaaa 2085

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&lt;210&gt; 93

&lt;211&gt; 301

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 93

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Met Ala Ser Ala Ala Arg Glu Leu Val Ile Gln Arg Leu Ser Leu Val
 1          5          10          15
Arg Ser Leu Cys Glu Ser Glu Glu Gln Arg Leu Leu Glu Gln Val His
 20          25          30
Gly Glu Glu Glu Arg Ala His Gln Ser Ile Leu Thr Gln Arg Val His
 35          40          45
Trp Ala Glu Ala Leu Gln Lys Leu Asp Thr Ile Arg Thr Gly Leu Val
 50          55          60
Gly Met Leu Thr His Leu Asp Asp Leu Gln Leu Ile Gln Lys Glu Gln
 65          70          75          80
Glu Ile Phe Glu Arg Thr Glu Glu Ala Glu Gly Ile Leu Asp Pro Gln
 85          90          95
Glu Ser Glu Met Leu Asn Phe Asn Glu Lys Cys Thr Arg Ser Pro Leu
100          105          110
Leu Thr Gln Leu Trp Ala Thr Ala Val Leu Gly Ser Leu Ser Gly Thr
115          120          125
Glu Asp Ile Arg Ile Asp Glu Arg Thr Val Ser Pro Phe Leu Gln Leu
130          135          140
Ser Asp Asp Arg Lys Thr Leu Thr Phe Ser Thr Lys Lys Ser Lys Ala
145          150          155          160
Cys Ala Asp Gly Pro Glu Arg Phe Asp His Trp Pro Asn Ala Leu Ala
165          170          175
Ala Thr Ser Phe Gln Asn Gly Leu His Ala Trp Met Val Asn Val Gln
180          185          190
Asn Ser Cys Ala Tyr Lys Val Gly Val Ala Ser Gly His Leu Pro Arg
195          200          205
Lys Gly Ser Gly Ser Asp Cys Arg Leu Gly His Asn Ala Phe Ser Trp
210          215          220
Val Phe Ser Arg Tyr Asp Gln Glu Phe Arg Phe Ser His Asn Gly Gln
225          230          235          240

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111

His	Glu	Pro	Leu	Gly	Leu	Leu	Arg	Gly	Pro	Ala	Gln	Leu	Gly	Val	Val
			245						250					255	
Leu	Asp	Leu	Gln	Val	Gln	Glu	Leu	Leu	Phe	Tyr	Glu	Pro	Ala	Ser	Gly
			260					265					270		
Ile	Val	Leu	Cys	Ala	His	His	Val	Ser	Phe	Pro	Gly	Pro	Leu	Phe	Pro
			275				280					285			
Val	Phe	Ala	Val	Ala	Asp	Gln	Thr	Ile	Ser	Ile	Val	Arg			
			290				295					300			

&lt;210&gt; 94

&lt;211&gt; 2317

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 94

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gacactcttg tcccttgga aaaaaaaaa aaaaaaa 2317

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&lt;210&gt; 95

&lt;211&gt; 626

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 95

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Met Val Asp Val Val Gly Leu Glu Arg Glu Thr Gly Pro Arg Gly Ser
 1          5          10          15
Pro Trp Pro Gly Leu Pro Leu Pro Ser Leu Val Gly Pro Ala Pro Leu
      20          25          30
Leu Thr Cys Leu Cys Pro Gln Cys Leu Ser Val Glu Asp Ala Leu Gly
      35          40          45
Leu Gly Glu Pro Glu Gly Ser Gly Leu Pro Pro Gly Pro Val Leu Glu
      50          55          60
Ala Arg Tyr Val Ala Arg Leu Ser Ala Ala Val Leu Tyr Leu Ser
      65          70          75          80
Asn Pro Glu Gly Thr Cys Glu Asp Ala Arg Ala Gly Leu Trp Ala Ser
      85          90          95
His Ala Asp His Leu Leu Ala Leu Leu Glu Ser Pro Lys Ala Leu Thr
      100          105          110
Pro Gly Leu Ser Trp Leu Leu Gln Arg Met Gln Ala Arg Ala Ala Gly
      115          120          125
Gln Thr Pro Lys Thr Ala Cys Val Asp Ile Pro Gln Leu Leu Glu Glu
      130          135          140
Ala Val Gly Ala Gly Ala Pro Gly Ser Ala Gly Gly Val Leu Ala Ala
      145          150          155          160
Leu Leu Asp His Val Arg Ser Gly Ser Cys Phe His Ala Leu Pro Ser
      165          170          175
Pro Gln Tyr Phe Val Asp Phe Val Phe Gln Gln His Ser Ser Glu Val
      180          185          190
Pro Met Thr Leu Ala Glu Leu Ser Ala Leu Met Gln Arg Leu Gly Val
      195          200          205
Gly Arg Glu Ala His Ser Asp His Ser His Arg His Arg Gly Ala Ser
      210          215          220
Ser Arg Asp Pro Val Pro Leu Ile Ser Ser Ser Asn Ser Ser Ser Val
      225          230          235          240
Trp Asp Thr Val Cys Leu Ser Ala Arg Asp Val Met Ala Ala Tyr Gly
      245          250          255
Leu Ser Glu Gln Ala Gly Val Thr Pro Glu Ala Trp Ala Gln Leu Ser
      260          265          270
Pro Ala Leu Leu Gln Gln Gln Leu Ser Gly Ala Tyr Thr Ser Gln Ser
      275          280          285
Arg Pro Pro Val Gln Asp Gln Leu Ser Gln Ser Glu Arg Tyr Leu Tyr
      290          295          300
Gly Ser Leu Ala Thr Leu Leu Ile Cys Leu Cys Ala Val Phe Gly Leu
      305          310          315          320
Leu Leu Leu Thr Cys Thr Gly Cys Arg Gly Val Ala His Tyr Ile Leu
      325          330          335
Gln Thr Phe Leu Ser Leu Ala Val Gly Ala Leu Thr Gly Asp Ala Val
      340          345          350
Leu His Leu Thr Pro Lys Val Leu Gly Leu His Thr His Ser Glu Glu
      355          360          365
Gly Leu Ser Pro Gln Pro Thr Trp Arg Leu Leu Ala Met Leu Ala Gly
      370          375          380
Leu Tyr Ala Phe Phe Leu Phe Glu Asn Leu Phe Asn Leu Leu Leu Pro
      385          390          395          400
Arg Asp Pro Glu Asp Leu Glu Asp Gly Pro Cys Gly His Ser Ser His
      405          410          415
Ser His Gly Gly His Ser His Gly Val Ser Leu Gln Leu Ala Pro Ser
      420          425          430

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113

Glu Leu Arg Gln Pro Lys Pro Pro His Glu Gly Ser Arg Ala Asp Leu  
           435                                  440                                  445  
 Val Ala Glu Glu Ser Pro Glu Leu Leu Asn Pro Glu Pro Arg Arg Leu  
           450                                  455                                  460  
 Ser Pro Glu Leu Arg Leu Leu Pro Tyr Met Ile Thr Leu Gly Asp Ala  
 465                                  470                                  475                                  480  
 Val His Asn Phe Ala Asp Gly Leu Ala Val Gly Ala Ala Phe Ala Ser  
                                   485                                  490                                  495  
 Ser Trp Lys Thr Gly Leu Ala Thr Ser Leu Ala Val Phe Cys His Glu  
                                   500                                  505                                  510  
 Leu Pro His Glu Leu Gly Asp Phe Ala Ala Leu Leu His Ala Gly Leu  
                                   515                                  520                                  525  
 Ser Val Arg Gln Ala Leu Leu Asn Leu Ala Ser Ala Leu Thr Ala  
                                   530                                  535                                  540  
 Phe Ala Gly Leu Thr Trp His Ser Arg Leu Glu Ser Ala Arg Arg Ala  
 545                                  550                                  555                                  560  
 Arg Pro Gly Ser Trp Gln Trp Pro Pro Ala Cys Ser Leu Arg Ser Thr  
                                   565                                  570                                  575  
 Leu Arg His Ala Pro Gly Asp Val Glu Ser Thr Gly Pro Ala Ala Pro  
                                   580                                  585                                  590  
 Gly Ser Ser Ser Cys Cys Thr Thr Trp Ala Cys Trp Ala Ala Gly Pro  
                                   595                                  600                                  605  
 Ser Cys Cys Cys Cys Pro Cys Thr Arg Met Thr Ser Pro Ser Asp Thr  
                                   610                                  615                                  620  
 Leu Pro  
 625

&lt;210&gt; 96

&lt;211&gt; 2761

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 96

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114

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&lt;210&gt; 97

&lt;211&gt; 422

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 97

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      35          40          45
Ala Thr Leu Ser Lys Val Glu Gly Thr Asp Val Thr Gly Ile Glu Glu
      50          55          60
Val Val Ile Pro Lys Lys Lys Thr Trp Asp Lys Val Ala Val Leu Gln
      65          70          75          80
Ala Leu Ala Ser Thr Val Asn Arg Asp Thr Thr Ala Val Pro Tyr Val
      85          90          95
Phe Gln Asp Asp Pro Tyr Leu Met Pro Ala Ser Ser Leu Glu Ser Arg
      100          105          110
Ser Phe Leu Leu Ala Lys Lys Ser Gly Glu Asn Val Ala Lys Phe Ile
      115          120          125
Ile Asn Ser Tyr Pro Lys Tyr Phe Gln Lys Asp Ile Ala Glu Pro His
      130          135          140
Ile Pro Cys Leu Met Pro Glu Tyr Phe Glu Pro Gln Ile Lys Asp Ile
      145          150          155          160
Ser Glu Ala Ala Leu Lys Glu Arg Ile Glu Leu Arg Lys Val Lys Ala
      165          170          175
Ser Val Asp Met Phe Asp Gln Leu Leu Gln Ala Gly Thr Thr Val Ser
      180          185          190
Leu Glu Thr Thr Asn Ser Leu Leu Asp Leu Leu Cys Tyr Tyr Gly Asp
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Gln Glu Pro Ser Thr Asp Tyr His Phe Gln Gln Thr Gly Gln Ser Glu
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115

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 Ser Leu Met Pro Glu Lys Asn Glu His Ser Tyr Cys Thr Met Ile Arg  
 260 265 270  
 Gly Met Val Lys His Arg Ala Tyr Glu Gln Ala Leu Asn Leu Tyr Thr  
 275 280 285  
 Glu Leu Leu Asn Asn Arg Leu His Ala Asp Val Tyr Thr Phe Asn Ala  
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 Leu Ile Glu Ala Thr Val Cys Ala Ile Asn Glu Lys Phe Glu Glu Lys  
 305 310 315 320  
 Trp Ser Lys Ile Leu Glu Leu Leu Arg His Met Val Ala Gln Lys Val  
 325 330 335  
 Lys Pro Asn Leu Gln Thr Phe Asn Thr Ile Leu Lys Cys Leu Arg Arg  
 340 345 350  
 Phe His Val Phe Ala Arg Ser Pro Ala Leu Gln Val Leu Arg Glu Met  
 355 360 365  
 Lys Ala Ile Gly Ile Glu Pro Ser Leu Ala Thr Tyr His His Ile Ile  
 370 375 380  
 Arg Leu Phe Asp Gln Pro Gly Asp Pro Leu Lys Arg Ser Ser Phe Ile  
 385 390 395 400  
 Ile Tyr Asp Ile Met Asn Glu Leu Met Gly Lys Arg Phe Ser Pro Lys  
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 Asp Pro Asp Asp Gly Ile  
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&lt;210&gt; 98

&lt;211&gt; 2757

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 98

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&lt;210&gt; 99

&lt;211&gt; 697

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 99

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Ala Gly Ser Ala Glu Lys Ser Lys Met Ala Val Val Ser Ala Val Arg
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Trp Leu Gly Leu Arg Ser Arg Leu Gly Gln Pro Leu Thr Gly Arg Arg
      20           25           30
Ala Gly Leu Cys Glu Gln Ala Arg Ser Cys Arg Phe Tyr Ser Gly Ser
      35           40           45
Ala Thr Leu Ser Lys Val Glu Gly Thr Asp Val Thr Gly Ile Glu Glu
      50           55           60
Val Val Ile Pro Lys Lys Lys Thr Trp Asp Lys Val Ala Val Leu Gln
      65           70           75           80
Ala Leu Ala Ser Thr Val Asn Arg Asp Thr Thr Ala Val Pro Tyr Val
      85           90           95
Phe Gln Asp Asp Pro Tyr Leu Met Pro Ala Ser Ser Leu Glu Ser Arg
      100          105          110
Ser Phe Leu Leu Ala Lys Lys Ser Gly Glu Asn Val Ala Lys Phe Ile
      115          120          125
Ile Asn Ser Tyr Pro Lys Tyr Phe Gln Lys Asp Ile Ala Glu Pro His
      130          135          140
Ile Pro Cys Leu Met Pro Glu Tyr Phe Glu Pro Gln Ile Lys Asp Ile
      145          150          155          160
Ser Glu Ala Ala Leu Lys Glu Arg Ile Glu Leu Arg Lys Val Lys Ala
      165          170          175
Ser Val Asp Met Phe Asp Gln Leu Leu Gln Ala Gly Thr Thr Val Ser
      180          185          190
Leu Glu Thr Thr Asn Ser Leu Leu Asp Leu Leu Cys Tyr Tyr Gly Asp
      195          200          205
Gln Glu Pro Ser Thr Asp Tyr His Phe Gln Gln Thr Gly Gln Ser Glu
      210          215          220
Ala Leu Glu Glu Glu Asn Asp Glu Thr Ser Arg Arg Lys Ala Gly His

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			260					265					270	Arg
Gly	Met	Val	Lys	His	Arg	Ala	Tyr	Glu	Gln	Ala	Leu	Asn	Leu	Tyr
		275					280					285		Thr
Glu	Leu	Leu	Asn	Asn	Arg	Leu	His	Ala	Asp	Val	Tyr	Thr	Phe	Asn
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Leu	Ile	Glu	Ala	Thr	Val	Cys	Ala	Ile	Asn	Glu	Lys	Phe	Glu	Glu
	305				310					315				Lys
Trp	Ser	Lys	Ile	Leu	Glu	Leu	Leu	Arg	His	Met	Val	Ala	Gln	Lys
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Lys	Pro	Asn	Leu	Gln	Thr	Phe	Asn	Thr	Ile	Leu	Lys	Cys	Leu	Arg
			340					345					350	Arg
Phe	His	Val	Phe	Ala	Arg	Ser	Pro	Ala	Leu	Gln	Val	Leu	Arg	Glu
	355					360					365			Met
Lys	Ala	Ile	Gly	Ile	Glu	Pro	Ser	Leu	Ala	Thr	Tyr	His	His	Ile
	370				375						380			Ile
Arg	Leu	Phe	Asp	Gln	Pro	Gly	Asp	Pro	Leu	Lys	Arg	Ser	Ser	Phe
	385			390						395				Ile
Ile	Tyr	Asp	Ile	Met	Asn	Glu	Leu	Met	Gly	Lys	Arg	Phe	Ser	Pro
			405						410					Lys
Asp	Pro	Asp	Asp	Asp	Lys	Phe	Phe	Gln	Ser	Ala	Met	Ser	Ile	Cys
		420						425					430	Ser
Ser	Leu	Arg	Asp	Leu	Glu	Leu	Ala	Tyr	Gln	Val	His	Gly	Leu	Leu
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Tyr	Tyr	Ser	Lys	Phe	Phe	Asp	Leu	Ile	Cys	Leu	Met	Glu	Gln	Ile
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Val	Thr	Leu	Lys	Trp	Tyr	Glu	Asp	Leu	Ile	Pro	Ser	Ala	Tyr	Phe
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Arg	Leu	Glu	Val	Ile	Pro	Lys	Ile	Trp	Lys	Asp	Ser	Lys	Glu	Tyr
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Arg	Asp	Lys	His	Pro	Pro	Glu	Leu	Gln	Val	Ala	Phe	Ala	Asp	Cys
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Ala	Asp	Ile	Lys	Ser	Ala	Tyr	Glu	Ser	Gln	Pro	Ile	Arg	Gln	Thr
			565						570					Ala
Gln	Asp	Trp	Pro	Ala	Thr	Ser	Leu	Asn	Cys	Ile	Ala	Ile	Leu	Phe
		580						585					590	Leu
Arg	Ala	Gly	Arg	Thr	Gln	Glu	Ala	Trp	Lys	Met	Leu	Gly	Leu	Phe
	595					600						605		Arg
Lys	His	Asn	Lys	Ile	Pro	Arg	Ser	Glu	Leu	Leu	Asn	Glu	Leu	Met
	610				615						620			Asp
Ser	Ala	Lys	Val	Ser	Asn	Ser	Pro	Ser	Gln	Ala	Ile	Glu	Val	Val
	625			630					635					Glu
Leu	Ala	Ser	Ala	Phe	Ser	Leu	Pro	Ile	Cys	Glu	Gly	Leu	Thr	Gln
			645					650						Arg
Val	Met	Ser	Asp	Phe	Ala	Ile	Asn	Gln	Glu	Gln	Lys	Glu	Ala	Leu
		660					665						670	Ser
Asn	Leu	Thr	Ala	Leu	Thr	Ser	Asp	Ser	Asp	Thr	Asp	Ser	Ser	Ser
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690

695

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 <213> Homo sapiens

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 tagataaatg ttgtaattag tgtacacgtt tgtatttttg ttaatatagc cgctgccata 1920  
 gttttctaac ttgaacagcc 1940

<210> 101  
 <211> 280  
 <212> PRT  
 <213> Homo sapiens

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 Gly Asp Asn Trp Lys Phe Ile Gly Pro Asp Gln His Arg Asn Phe Tyr  
 35 40 45  
 Tyr Ser Lys Phe Phe Asp Leu Ile Cys Leu Met Glu Gln Ile Asp Val  
 50 55 60  
 Thr Leu Lys Trp Tyr Glu Asp Leu Ile Pro Ser Ala Tyr Phe Pro His

119

65		70		75		80									
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Leu	Glu	Val	Ile	Pro	Lys	Ile	Trp	Lys	Asp	Ser	Lys	Glu	Tyr	Gly	His
			100						105					110	
Thr	Phe	Arg	Ser	Asp	Leu	Arg	Glu	Glu	Ile	Leu	Met	Leu	Met	Ala	Arg
			115						120					125	
Asp	Lys	His	Pro	Pro	Glu	Leu	Gln	Val	Ala	Phe	Ala	Asp	Cys	Ala	Ala
			130						135					140	
Asp	Ile	Lys	Ser	Ala	Tyr	Glu	Ser	Gln	Pro	Ile	Arg	Gln	Thr	Ala	Gln
			145						150					155	
Asp	Trp	Pro	Ala	Thr	Ser	Leu	Asn	Cys	Ile	Ala	Ile	Leu	Phe	Leu	Arg
			165						170					175	
Ala	Gly	Arg	Thr	Gln	Glu	Ala	Trp	Lys	Met	Leu	Gly	Leu	Phe	Arg	Lys
			180						185					190	
His	Asn	Lys	Ile	Pro	Arg	Ser	Glu	Leu	Leu	Asn	Glu	Leu	Met	Asp	Ser
			195						200					205	
Ala	Lys	Val	Ser	Asn	Ser	Pro	Ser	Gln	Ala	Ile	Glu	Val	Val	Glu	Leu
			210						215					220	
Ala	Ser	Ala	Phe	Ser	Leu	Pro	Ile	Cys	Glu	Gly	Leu	Thr	Gln	Arg	Val
			225						230					235	
Met	Ser	Asp	Phe	Ala	Ile	Asn	Gln	Glu	Gln	Lys	Glu	Ala	Leu	Ser	Asn
			245						250					255	
Leu	Thr	Ala	Leu	Thr	Ser	Asp	Ser	Asp	Thr	Asp	Ser	Ser	Ser	Asp	Ser
			260						265					270	
Asp	Ser	Asp	Thr	Ser	Glu	Gly	Lys								
			275				280								

&lt;210&gt; 102

&lt;211&gt; 1853

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 102

```

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120

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&lt;210&gt; 103

&lt;211&gt; 414

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 103

```

Met Ser Ser Pro Asp Ala Gly Tyr Ala Ser Asp Asp Gln Ser Gln Thr
 1          5          10          15
Gln Ser Ala Leu Pro Ala Val Met Ala Gly Leu Gly Pro Cys Pro Trp
          20          25          30
Ala Glu Ser Leu Ser Pro Ile Gly Asp Met Lys Val Lys Gly Glu Ala
          35          40          45
Pro Ala Asn Ser Gly Ala Pro Ala Gly Ala Ala Gly Arg Ala Lys Gly
          50          55          60
Glu Ser Arg Ile Arg Arg Pro Met Asn Ala Phe Met Val Trp Ala Lys
          65          70          75          80
Asp Glu Arg Lys Arg Leu Ala Gln Gln Asn Pro Asp Leu His Asn Ala
          85          90          95
Glu Leu Ser Lys Met Leu Gly Lys Ser Trp Lys Ala Leu Thr Leu Ala
          100          105          110
Glu Lys Arg Pro Phe Val Glu Glu Ala Glu Arg Leu Arg Val Gln His
          115          120          125
Met Gln Asp His Pro Asn Tyr Lys Tyr Arg Pro Arg Arg Arg Lys Gln
          130          135          140
Val Lys Arg Leu Lys Arg Val Glu Gly Gly Phe Leu His Gly Leu Ala
          145          150          155          160
Glu Pro Gln Ala Ala Ala Leu Gly Pro Glu Gly Gly Arg Val Ala Met
          165          170          175
Asp Gly Leu Gly Leu Gln Phe Pro Glu Gln Gly Phe Pro Ala Gly Pro
          180          185          190
Pro Leu Leu Pro Pro His Met Gly Gly His Tyr Arg Asp Cys Gln Ser
          195          200          205
Leu Gly Ala Pro Pro Leu Asp Gly Tyr Pro Leu Pro Thr Pro Asp Thr
          210          215          220
Ser Pro Leu Asp Gly Val Asp Pro Asp Pro Ala Phe Phe Ala Ala Pro
          225          230          235          240
Met Pro Gly Asp Cys Pro Ala Ala Gly Thr Tyr Ser Tyr Ala Gln Val
          245          250          255
Ser Asp Tyr Ala Gly Pro Pro Glu Pro Pro Ala Gly Pro Met His Pro
          260          265          270
Arg Leu Gly Pro Glu Pro Ala Gly Pro Ser Ile Pro Gly Leu Leu Ala
          275          280          285
Pro Pro Ser Ala Leu His Val Tyr Tyr Gly Ala Met Gly Ser Pro Gly
          290          295          300
Ala Gly Gly Gly Arg Gly Phe Gln Met Gln Pro Gln His Gln His Gln
          305          310          315          320
His Gln His Gln His His Pro Pro Gly Pro Gly Gln Pro Ser Pro Pro
          325          330          335
Pro Glu Ala Leu Pro Cys Arg Asp Gly Thr Asp Pro Ser Gln Pro Ala

```

121

340	345	350
Glu Leu Leu Gly Glu Val Asp Arg Thr Glu Phe Glu Gln Tyr Leu His		
355	360	365
Phe Val Cys Lys Pro Glu Met Gly Leu Pro Tyr Gln Gly His Asp Ser		
370	375	380
Gly Val Asn Leu Pro Asp Ser His Gly Ala Ile Ser Ser Val Val Ser		
385	390	395
Asp Ala Ser Ser Ala Val Tyr Tyr Cys Asn Tyr Pro Asp Val		400
405	410	

&lt;210&gt; 104

&lt;211&gt; 2398

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 104

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cgcctcagcc tcatgagtag ctgggactac aggtgtgggt gtccacgcc agctaatttt 180
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122

<210> 105  
 <211> 232  
 <212> PRT  
 <213> Homo sapiens

<400> 105  
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 20 25 30  
 Met Glu Lys Thr Pro His Cys Phe Leu Thr Asp Gln Gly Ala Ala Gln  
 35 40 45  
 Phe Ala Ala Ala Met Gly Val Pro Glu Ile Pro Gly Glu Lys Leu Val  
 50 55 60  
 Thr Glu Arg Asn Lys Lys Arg Leu Glu Lys Glu Lys His Glu Lys Gly  
 65 70 75 80  
 Ala Gln Lys Thr Asp Cys Gln Lys Asn Leu Gly Thr Val Gly Ala Val  
 85 90 95  
 Ala Leu Asp Cys Lys Gly Asn Val Ala Tyr Ala Thr Ser Thr Gly Gly  
 100 105 110  
 Ile Val Asn Lys Met Val Gly Arg Val Gly Asp Ser Pro Cys Leu Gly  
 115 120 125  
 Ala Gly Gly Tyr Ala Asp Asn Asp Ile Gly Ala Val Ser Thr Thr Gly  
 130 135 140  
 His Gly Glu Ser Ile Leu Lys Val Asn Leu Ala Arg Leu Thr Leu Phe  
 145 150 155 160  
 His Ile Glu Gln Gly Lys Thr Val Glu Glu Ala Ala Asp Leu Ser Leu  
 165 170 175  
 Gly Tyr Met Lys Ser Arg Val Lys Gly Leu Gly Gly Leu Ile Val Val  
 180 185 190  
 Ser Lys Thr Gly Asp Trp Val Ala Lys Trp Thr Ser Thr Ser Met Pro  
 195 200 205  
 Trp Ala Ala Ala Lys Asp Gly Lys Leu His Phe Gly Ile Asp Pro Asp  
 210 215 220  
 Asp Thr Thr Ile Thr Asp Leu Pro  
 225 230

<210> 106  
 <211> 1811  
 <212> DNA  
 <213> Homo sapiens

<400> 106  
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 tattctggct ggagcaattg cactcatcat tggctttggg atttcaggga gacactccat 180  
 cacagtcact actgtcgcct cagctgggaa cattggggag gatggaatcc agagctgcac 240  
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 tatcaaagtg acagaatcgg agatcaaaag gcggagtcac ctacagctgc taaactcaaa 840

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aaactgattt tagagttctg atcgttcaag agaattgatta aatatacatt tcctaaaaaa 1800
aaaaaaaaa a 1811

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&lt;210&gt; 107

&lt;211&gt; 282

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 107

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Met Ala Ser Leu Gly Gln Ile Leu Phe Trp Ser Ile Ile Ser Ile Ile
1      5      10      15
Ile Ile Leu Ala Gly Ala Ile Ala Leu Ile Ile Gly Phe Gly Ile Ser
20     25     30
Gly Arg His Ser Ile Thr Val Thr Thr Val Ala Ser Ala Gly Asn Ile
35     40     45
Gly Glu Asp Gly Ile Gln Ser Cys Thr Phe Glu Pro Asp Ile Lys Leu
50     55     60
Ser Asp Ile Val Ile Gln Trp Leu Lys Glu Gly Val Leu Gly Leu Val
65     70     75     80
His Glu Phe Lys Glu Gly Lys Asp Glu Leu Ser Glu Gln Asp Glu Met
85     90     95
Phe Arg Gly Arg Thr Ala Val Phe Ala Asp Gln Val Ile Val Gly Asn
100    105    110
Ala Ser Leu Arg Leu Lys Asn Val Gln Leu Thr Asp Ala Gly Thr Tyr
115    120    125
Lys Cys Tyr Ile Ile Thr Ser Lys Gly Lys Gly Asn Ala Asn Leu Glu
130    135    140
Tyr Lys Thr Gly Ala Phe Ser Met Pro Glu Val Asn Val Asp Tyr Asn
145    150    155    160
Ala Ser Ser Glu Thr Leu Arg Cys Glu Ala Pro Arg Trp Phe Pro Gln
165    170    175
Pro Thr Val Val Trp Ala Ser Gln Val Asp Gln Gly Ala Asn Phe Ser
180    185    190
Glu Val Ser Asn Thr Ser Phe Glu Leu Asn Ser Glu Asn Val Thr Met
195    200    205
Lys Val Val Ser Val Leu Tyr Asn Val Thr Ile Asn Asn Thr Tyr Ser
210    215    220
Cys Met Ile Glu Asn Asp Ile Ala Lys Ala Thr Gly Asp Ile Lys Val
225    230    235    240
Thr Glu Ser Glu Ile Lys Arg Arg Ser His Leu Gln Leu Leu Asn Ser
245    250    255
Lys Ala Ser Leu Cys Val Ser Ser Phe Phe Ala Ile Ser Trp Ala Leu
260    265    270

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Leu Pro Leu Ser Pro Tyr Leu Met Leu Lys  
275 280

<210> 108  
<211> 2611  
<212> DNA  
<213> Homo sapiens

<400> 108  
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<210> 109  
<211> 150  
<212> PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 109

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Gln Asn Leu Ala Cys Phe Leu Thr Asn Pro His Cys Gly Ser Leu Val
          20           25           30
Asn Ala Asp Gly His Gly Glu Val Trp Thr Asp Trp Asn Asn Met Ser
          35           40           45
Lys Phe Phe Gln Tyr Gly Trp Arg Cys Thr Thr Asn Glu Asn Thr Tyr
          50           55           60
Ser Asn Arg Thr Leu Met Gly Asn Trp Asn Gln Glu Arg Tyr Asp Leu
65           70           75           80
Arg Asn Ile Val Gln Pro Lys Pro Leu Pro Ser Gln Phe Gly His Tyr
          85           90           95
Phe Glu Thr Thr Tyr Asp Thr Ser Tyr Asn Asn Lys Met Pro Leu Ser
          100          105          110
Thr His Arg Phe Lys Arg Glu Pro His Trp Phe Pro Gly His Gln Pro
          115          120          125
Glu Leu Asp Pro Pro Arg Tyr Lys Cys Thr Glu Lys Ser Thr Tyr Met
          130          135          140
Asn Ser Tyr Ser Lys Pro
145           150

```

&lt;210&gt; 110

&lt;211&gt; 1032

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 110

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acagctccca actatgttgt tctgtctcca tggtcggggc tctgacagcc actttgaata 1020
aaccagacac cg                                     1032

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&lt;210&gt; 111

&lt;211&gt; 257

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 111

```

Met Ala Gln Arg Met Thr Thr Gln Leu Leu Leu Leu Leu Val Trp Val
 1           5           10           15

```

126

Ala Val Val Gly Glu Ala Gln Thr Arg Ile Ala Trp Ala Arg Thr Glu  
 20 25 30  
 Leu Leu Asn Val Cys Met Asn Ala Lys His His Lys Glu Lys Pro Gly  
 35 40 45  
 Pro Glu Asp Lys Leu His Glu Gln Cys Arg Pro Trp Arg Lys Asn Ala  
 50 55 60  
 Cys Cys Ser Thr Asn Thr Ser Gln Glu Ala His Lys Asp Val Ser Tyr  
 65 70 75 80  
 Leu Tyr Arg Phe Asn Trp Asn His Cys Gly Glu Met Ala Pro Ala Cys  
 85 90 95  
 Lys Arg His Phe Ile Gln Asp Thr Cys Leu Tyr Glu Cys Ser Pro Asn  
 100 105 110  
 Leu Gly Pro Trp Ile Gln Gln Val Asp Gln Ser Trp Arg Lys Glu Arg  
 115 120 125  
 Val Leu Asn Val Pro Leu Cys Lys Glu Asp Cys Glu Gln Trp Trp Glu  
 130 135 140  
 Asp Cys Arg Thr Ser Tyr Thr Cys Lys Ser Asn Trp His Lys Gly Trp  
 145 150 155 160  
 Asn Trp Thr Ser Gly Phe Asn Lys Cys Ala Val Gly Ala Ala Cys Gln  
 165 170 175  
 Pro Phe His Phe Tyr Phe Pro Thr Pro Thr Val Leu Cys Asn Glu Ile  
 180 185 190  
 Trp Thr His Ser Tyr Lys Val Ser Asn Tyr Ser Arg Gly Ser Gly Arg  
 195 200 205  
 Cys Ile Gln Met Trp Phe Asp Pro Ala Gln Gly Asn Pro Asn Glu Glu  
 210 215 220  
 Val Ala Arg Phe Tyr Ala Ala Ala Met Ser Gly Ala Gly Pro Trp Ala  
 225 230 235 240  
 Ala Trp Pro Phe Leu Leu Ser Leu Ala Leu Met Leu Leu Trp Leu Leu  
 245 250 255  
 Ser

&lt;210&gt; 112

&lt;211&gt; 1104

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 112

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ccacttttgaa taaaccagac accg

1104

&lt;210&gt; 113

&lt;211&gt; 939

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 113

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aagccaggcc	ccgaggacaa	gttgcagtag	cagtgtcgac	cctggaggaa	gaatgcctgc	240
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&lt;210&gt; 114

&lt;211&gt; 1331

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 114

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tgggggtcgg	acaggttgaa	cggaaccct	gtgctctaaa	cagttagggt	ttgttcccgc	360
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ccagacaccg	c					1331

&lt;210&gt; 115

&lt;211&gt; 929

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 115

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accgcacatg tgtcttgaga attatttgg 929

```

&lt;210&gt; 116

&lt;211&gt; 858

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 116

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ccacatgaaa aaaaaaaaa 858

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&lt;210&gt; 117

&lt;211&gt; 243

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 117

```

Met Ala Trp Gln Met Met Gln Leu Leu Leu Leu Ala Leu Val Thr Ala
 1             5             10             15
Ala Gly Ser Ala Gln Pro Arg Ser Ala Arg Ala Arg Thr Asp Leu Leu
      20             25             30
Asn Val Cys Met Asn Ala Lys His His Lys Thr Gln Pro Ser Pro Glu
      35             40             45
Asp Glu Leu Tyr Gly Gln Cys Ser Pro Trp Lys Lys Asn Ala Cys Cys
      50             55             60
Thr Ala Ser Thr Ser Gln Glu Leu His Lys Asp Thr Ser Arg Leu Tyr
65             70             75             80

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[illegible]

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<210> 118
<211> 1362
<212> DNA
<213> Homo sapiens
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<400> 118						
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ttgggtgttcc	tcacctggcat	gcccatggag	ttctacagca	tcattctggaa	tccccctgacc	300
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<210> 119
<211> 453
<212> PRT
<213> Homo sapiens
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130

&lt;400&gt; 119

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His Ser His Val Pro Glu Phe Glu Val Ala Thr Trp Ile Lys Ile Thr
 20          25          30
Leu Ile Leu Val Tyr Leu Ile Ile Phe Val Met Gly Leu Leu Gly Asn
 35          40          45
Ser Ala Thr Ile Arg Val Thr Gln Val Leu Gln Lys Lys Gly Tyr Leu
 50          55          60
Gln Lys Glu Val Thr Asp His Met Val Ser Leu Ala Cys Ser Asp Ile
 65          70          75          80
Leu Val Phe Leu Ile Gly Met Pro Met Glu Phe Tyr Ser Ile Ile Trp
 85          90          95
Asn Pro Leu Thr Thr Ser Ser Tyr Thr Leu Ser Cys Lys Leu His Thr
 100          105          110
Phe Leu Phe Glu Ala Cys Ser Tyr Ala Thr Leu Leu His Val Leu Thr
 115          120          125
Leu Ser Phe Glu Arg Tyr Ile Ala Ile Cys His Pro Phe Arg Tyr Lys
 130          135          140
Ala Val Ser Gly Pro Cys Gln Val Lys Leu Leu Ile Gly Phe Val Trp
 145          150          155          160
Val Thr Ser Ala Leu Val Ala Leu Pro Leu Leu Phe Ala Met Gly Thr
 165          170          175
Glu Tyr Pro Leu Val Asn Val Pro Ser His Arg Gly Leu Thr Cys Asn
 180          185          190
Arg Ser Ser Thr Arg His His Glu Gln Pro Glu Thr Ser Asn Met Ser
 195          200          205
Ile Cys Thr Asn Leu Ser Ser Arg Trp Thr Val Phe Gln Ser Ser Ile
 210          215          220
Phe Gly Ala Phe Val Val Tyr Leu Val Val Leu Leu Ser Val Ala Phe
 225          230          235          240
Met Cys Trp Asn Met Met Gln Val Leu Met Lys Ser Gln Lys Gly Ser
 245          250          255
Leu Ala Gly Gly Thr Arg Pro Pro Gln Leu Arg Lys Ser Glu Ser Glu
 260          265          270
Glu Ser Arg Thr Ala Arg Arg Gln Thr Ile Ile Phe Leu Arg Leu Ile
 275          280          285
Val Val Thr Leu Ala Val Cys Trp Met Pro Asn Gln Ile Arg Arg Ile
 290          295          300
Met Ala Ala Ala Lys Pro Lys His Asp Trp Thr Arg Ser Tyr Phe Arg
 305          310          315          320
Ala Tyr Met Ile Leu Leu Pro Phe Ser Glu Thr Phe Phe Tyr Leu Ser
 325          330          335
Ser Val Ile Asn Pro Leu Leu Tyr Thr Val Ser Ser Gln Gln Phe Arg
 340          345          350
Arg Val Phe Val Gln Val Leu Cys Cys Arg Leu Ser Leu Gln His Ala
 355          360          365
Asn His Glu Lys Arg Leu Arg Val His Ala His Ser Thr Thr Asp Ser
 370          375          380
Ala Arg Phe Val Gln Arg Pro Leu Leu Phe Ala Ser Arg Arg Gln Ser
 385          390          395          400
Ser Ala Arg Arg Thr Glu Lys Ile Phe Leu Ser Thr Phe Gln Ser Glu
 405          410          415
Ala Glu Pro Gln Ser Lys Ser Gln Ser Leu Ser Leu Glu Ser Leu Glu
 420          425          430
Pro Asn Ser Gly Ala Lys Pro Ala Asn Ser Ala Ala Glu Asn Gly Phe
 435          440          445

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Gln Glu His Glu Val  
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<210> 120  
<211> 2870  
<212> DNA  
<213> Homo sapiens

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tgacggcatg gaatgtataa atgagggtgg gtccttctgc agatactcta atcactacat 2700  
tgctttttct ataaaactac ccataagcct ttaaccttta aagaaaaatg aaaaaggtta 2760  
gtgtttgggg gccgggggag gactgaccgc ttcataagcc agtacgtctg agctgagtat 2820  
gtttcaataa accttttgat atttctcaaa aaaaaaaaaa aaaaaaaaaa 2870

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<210> 121
<211> 403
<212> PRT
<213> Homo sapiens
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<400>	121														
Met	Phe	Val	Ala	Ser	Glu	Arg	Lys	Met	Arg	Ala	His	Gln	Val	Leu	Thr
1				5					10					15	
Phe	Leu	Leu	Leu	Phe	Val	Ile	Thr	Ser	Val	Ala	Ser	Glu	Asn	Ala	Ser
			20					25					30		
Thr	Ser	Arg	Gly	Cys	Gly	Leu	Asp	Leu	Leu	Pro	Gln	Tyr	Val	Ser	Leu
		35					40					45			
Cys	Asp	Leu	Asp	Ala	Ile	Trp	Gly	Ile	Val	Val	Glu	Ala	Val	Ala	Gly
	50					55					60				
Ala	Gly	Ala	Leu	Ile	Thr	Leu	Leu	Leu	Met	Leu	Ile	Leu	Leu	Val	Arg
65					70					75					80
Leu	Pro	Phe	Ile	Lys	Glu	Lys	Glu	Lys	Lys	Ser	Pro	Val	Gly	Leu	His
				85					90					95	
Phe	Leu	Phe	Leu	Leu	Gly	Thr	Leu	Gly	Leu	Phe	Gly	Leu	Thr	Phe	Ala
			100					105					110		
Phe	Ile	Ile	Gln	Glu	Asp	Glu	Thr	Ile	Cys	Ser	Val	Arg	Arg	Phe	Leu
		115					120					125			
Trp	Gly	Val	Leu	Phe	Ala	Leu	Cys	Phe	Ser	Cys	Leu	Leu	Ser	Gln	Ala
	130					135					140				
Trp	Arg	Val	Arg	Arg	Leu	Val	Arg	His	Gly	Thr	Gly	Pro	Ala	Gly	Trp
145					150					155					160
Gln	Leu	Val	Gly	Leu	Ala	Leu	Cys	Leu	Met	Leu	Val	Gln	Val	Ile	Ile
				165					170					175	
Ala	Val	Glu	Trp	Leu	Val	Leu	Thr	Val	Leu	Arg	Asp	Thr	Arg	Pro	Ala
			180					185					190		
Cys	Ala	Tyr	Glu	Pro	Met	Asp	Phe	Val	Met	Ala	Leu	Ile	Tyr	Asp	Met
		195					200					205			
Val	Leu	Leu	Val	Val	Thr	Leu	Gly	Leu	Ala	Leu	Phe	Thr	Leu	Cys	Gly
	210					215					220				
Lys	Phe	Lys	Arg	Trp	Lys	Leu	Asn	Gly	Ala	Phe	Leu	Leu	Ile	Thr	Ala
225					230					235					240
Phe	Leu	Ser	Val	Leu	Ile	Trp	Val	Ala	Trp	Met	Thr	Met	Tyr	Leu	Phe
				245					250					255	
Gly	Asn	Val	Lys	Leu	Gln	Gln	Gly	Asp	Ala	Trp	Asn	Asp	Pro	Thr	Leu
				260				265					270		
Ala	Ile	Thr	Leu	Ala	Ala	Ser	Gly	Trp	Val	Phe	Val	Ile	Phe	His	Ala
		275					280					285			
Ile	Pro	Glu	Ile	His	Cys	Thr	Leu	Leu	Pro	Ala	Leu	Gln	Glu	Asn	Thr
	290					295					300				
Pro	Asn	Tyr	Phe	Asp	Thr	Ser	Gln	Pro	Arg	Met	Arg	Glu	Thr	Ala	Phe
305					310					315					320
Glu	Glu	Asp	Val	Gln	Leu	Pro	Arg	Ala	Tyr	Met	Glu	Asn	Lys	Ala	Phe
				325					330					335	
Ser	Met	Asp	Glu	His	Asn	Ala	Ala	Leu	Arg	Thr	Ala	Gly	Phe	Pro	Asn

133

<210> 122  
 <211> 1474  
 <212> DNA  
 <213> Homo sapiens

<400> 122  
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 caccaccacc aggtaattgg ccttatcagc tctgtgcctg tctccagtca ggctggaata 120  
 agtctcctca tatgtgcaag ctcgccctc ccctggaatc taaagcctcc tcagccttct 180  
 gagtccacct gaaaggaaaca ggccgaactg ctgtatgggc tctactgccca gtgtgacctc 240  
 accctctcca gtcacccctc ctccagttcca gctatgagtt cctgcaactt cacacatgcc 300  
 acctgtgtgc ttattggtat cccaggatta gagaaagccc atttctgggt tggcttcccc 360  
 ctcttttcca tgtatgtagt ggcaatgtgt ggaaactgca tcgtgggtctt catcgtaagg 420  
 acggaacgca gcctgcacgc tccgatgtac ctctttctct gcatgcttgc agccattgac 480  
 ctggccttat ccacatccac catgcctaag atccttgccc ttttctgggt tgattccccga 540  
 gagattagca ttgaggcctg tcttaccagc atgttcttta ttcatgccct ctcagccatt 600  
 gaatccacca tctgtctggc catggccttt gaccgttatg tggccatctg ccaccactg 660  
 cgccatgctg cagtgtctca caatacagta acagcccaga ttggcatcgt ggctgtggtc 720  
 cgcgatcccc tctttttttt cccactgcct ctgctgatca agcggtctggc cttctgccac 780  
 tccaatgtcc tctcgcactc ctattgtgtc caccaggatg taatgaagtt ggcctatgca 840  
 gacactttgc ccaatgtggt atatggtctt actgccattc tgctgggtcat gggcggtggac 900  
 gtaatgttca tctccttgtc ctattttctg ataatacga cggttctgca actgccttcc 960  
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 ttctatgtgc cacttatggc cctctcagtt gtacaccgct ttgaaaacag ctttcatccc 1080  
 attgtgcgtg ttgtcatggg tgacatctac ctgctgctgc ctctgtcat caatcccatc 1140  
 atctatggtg ccaaaaccaa acagatcaga acacgggtgc tggctatgtt caagatcagc 1200  
 tgtgacaagg acttgaggc tgtgggaggc aagtgaccct taacactaca cttctcctta 1260  
 tctttattgg cttgataaac ataattattt ctaacactag cttatttcca gttgcccata 1320  
 agcacatcag tacttttctc tggctggaat agtaaaactaa agtatggtac atctacctaa 1380  
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 aaaaccaaac atgcttataa cattaaaaaa aaaa 1474

<210> 123  
 <211> 320  
 <212> PRT  
 <213> Homo sapiens

<400> 123  
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 1 5 10 15  
 Pro Gly Leu Glu Lys Ala His Phe Trp Val Gly Phe Pro Leu Leu Ser  
 20 25 30  
 Met Tyr Val Val Ala Met Cys Gly Asn Cys Ile Val Val Phe Ile Val  
 35 40 45  
 Arg Thr Glu Arg Ser Leu His Ala Pro Met Tyr Leu Phe Leu Cys Met  
 50 55 60  
 Leu Ala Ala Ile Asp Leu Ala Leu Ser Thr Ser Thr Met Pro Lys Ile  
 65 70 75 80  
 Leu Ala Leu Phe Trp Phe Asp Ser Arg Glu Ile Ser Ile Glu Ala Cys  
 85 90 95  
 Leu Thr Gln Met Phe Phe Ile His Ala Leu Ser Ala Ile Glu Ser Thr  
 100 105 110  
 Ile Leu Leu Ala Met Ala Phe Asp Arg Tyr Val Ala Ile Cys His Pro  
 115 120 125  
 Leu Arg His Ala Ala Val Leu Asn Asn Thr Val Thr Ala Gln Ile Gly

134

130		135		140
Ile Val Ala Val Val Arg Gly Ser Leu Phe Phe		Phe Pro Leu Pro Leu		
145		150		155
Leu Ile Lys Arg Leu Ala Phe Cys His Ser Asn Val Leu Ser His Ser				160
		165		170
Tyr Cys Val His Gln Asp Val Met Lys Leu Ala Tyr Ala Asp Thr Leu				175
		180		185
Pro Asn Val Val Tyr Gly Leu Thr Ala Ile Leu Leu Val Met Gly Val				190
		195		200
Asp Val Met Phe Ile Ser Leu Ser Tyr Phe Leu Ile Ile Arg Thr Val				205
		210		215
Leu Gln Leu Pro Ser Lys Ser Glu Arg Ala Lys Ala Phe Gly Thr Cys				220
225		230		235
Val Ser His Ile Gly Val Val Leu Ala Phe Tyr Val Pro Leu Ile Gly				240
		245		250
Leu Ser Val Val His Arg Phe Gly Asn Ser Leu His Pro Ile Val Arg				255
		260		265
Val Val Met Gly Asp Ile Tyr Leu Leu Leu Pro Pro Val Ile Asn Pro				270
		275		280
Ile Ile Tyr Gly Ala Lys Thr Lys Gln Ile Arg Thr Arg Val Leu Ala				285
		290		295
Met Phe Lys Ile Ser Cys Asp Lys Asp Leu Gln Ala Val Gly Gly Lys				300
305		310		315
				320

&lt;210&gt; 124

&lt;211&gt; 2205

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 124

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gccagacttc ggaacgggtg tcttgctact cctgctgggg ctccctcagg acaagggcac 180
acaactgggt ccgttaagcc cctctctcgc tcagacgcca tggagctgga tctgtctcca 240
cctcatctta gcagctctcc ggaagacctt tggccagccc ctgggacccc tcttgggact 300
ccccggcccc ctgatacccc tctgcctgag gaggtaaaga ggtcccagcc tctcctcatc 360
ccaaccacog gcaggaaact tcgagaggag gagaggcgtg ccacctccct cccctctatc 420
cccaaccctt tccctgagct ctgcagtcct ccctcacaga gccaattct cgggggcccc 480
tccagtgcaa gggggtgct ccccgcat gccagccgcc cccatgtagt aaaggtgtac 540
agtgaggatg gggcctgcag gtctgtggag gtggcagcag gtgccacagc tcgccacgtg 600
tgtgaaatgc tgggtgcagc agctcacgcc ttgagcgacg agacctgggg gctggtggag 660
tgccaccccc acctagcact ggagcggggt ttggaggacc acgagtcctg ggtggaagtg 720
caggctgcct ggcccgtggg cggagatagc cgcttcgtct tccggaaaaa cttcgccaag 780
tacgaactgt tcaagagctc cccacactcc ctgttcccag aaaaaatggt ctccagctgt 840
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cagggccgca agctctacgg gatgccact gacttcggtt tctgtgtcaa gcccaacaag 1140
cttcgaaatg gacacaaggg gcttcggatc ttctgcagtg aagatgagca gagccgcacc 1200
tgctggctgg ctgccttccg cctcttcaag tacggggtgc agctgtacaa gaattaccag 1260
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acccaactct ggttcacagg gcgcatttcc cgtgaggaga gccagcggtt tattggacag 1560
cagggcttgg tagacggcct gttcctggtc cgggagagtc agcggaaccc ccagggcttt 1620

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135

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gtcctctctt tgtgccacct gcagaaagt aagcattatc tcatcctgcc gagcgaggag 1680
gagggtcgcc tgtacttcag catggatgat ggccagaccc gcttcaactga cctgctgcag 1740
ctcgtggagt tccaccagct gaaccgcggc atcctgccgt gcttgctgcg ccattgctgc 1800
acgcgggtgg ccctctgacc aggccgtgga ctggctcatg cctcagcccg ccttcagget 1860
gcccggcgcc cctccacca tccagtggac tctggggcgc ggccacagg gacgggatga 1920
ggagcgggag ggttccgcc ctccagtttt ctcctctgct tctttgcctc cctcagatag 1980
aaaacagccc ccaactccagt ccaactcctga cccctctcct caagggaagg ccttggtggtg 2040
ccccctctcc ttctcctagc tctggaggtg ctgctctagg gcagggaatt atgggagaag 2100
tgggggcagc ccaggcggtt tcacgcccc cactttgtac agaccgagag gccagttgat 2160
ctgctctgtt ttatactagt gacaataaag attatttttt gatac 2205

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&lt;210&gt; 125

&lt;211&gt; 532

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 125

```

Met Glu Leu Asp Leu Ser Pro Pro His Leu Ser Ser Ser Pro Glu Asp
1      5      10      15
Leu Trp Pro Ala Pro Gly Thr Pro Pro Gly Thr Pro Arg Pro Pro Asp
20     25     30
Thr Pro Leu Pro Glu Glu Val Lys Arg Ser Gln Pro Leu Leu Ile Pro
35     40     45
Thr Thr Gly Arg Lys Leu Arg Glu Glu Glu Arg Arg Ala Thr Ser Leu
50     55     60
Pro Ser Ile Pro Asn Pro Phe Pro Glu Leu Cys Ser Pro Pro Ser Gln
65     70     75     80
Ser Pro Ile Leu Gly Gly Pro Ser Ser Ala Arg Gly Leu Leu Pro Arg
85     90     95
Asp Ala Ser Arg Pro His Val Val Lys Val Tyr Ser Glu Asp Gly Ala
100    105    110
Cys Arg Ser Val Glu Val Ala Ala Gly Ala Thr Ala Arg His Val Cys
115    120    125
Glu Met Leu Val Gln Arg Ala His Ala Leu Ser Asp Glu Thr Trp Gly
130    135    140
Leu Val Glu Cys His Pro His Leu Ala Leu Glu Arg Gly Leu Glu Asp
145    150    155    160
His Glu Ser Val Val Glu Val Gln Ala Ala Trp Pro Val Gly Gly Asp
165    170    175
Ser Arg Phe Val Phe Arg Lys Asn Phe Ala Lys Tyr Glu Leu Phe Lys
180    185    190
Ser Ser Pro His Ser Leu Phe Pro Glu Lys Met Val Ser Ser Cys Leu
195    200    205
Asp Ala His Thr Gly Ile Ser His Glu Asp Leu Ile Gln Asn Phe Leu
210    215    220
Asn Ala Gly Ser Phe Pro Glu Ile Gln Gly Phe Leu Gln Leu Arg Gly
225    230    235    240
Ser Gly Arg Lys Leu Trp Lys Arg Phe Phe Cys Phe Leu Arg Arg Ser
245    250    255
Gly Leu Tyr Tyr Ser Thr Lys Gly Thr Ser Lys Asp Pro Arg His Leu
260    265    270
Gln Tyr Val Ala Asp Val Asn Glu Ser Asn Val Tyr Val Val Thr Gln
275    280    285
Gly Arg Lys Leu Tyr Gly Met Pro Thr Asp Phe Gly Phe Cys Val Lys
290    295    300
Pro Asn Lys Leu Arg Asn Gly His Lys Gly Leu Arg Ile Phe Cys Ser
305    310    315    320
Glu Asp Glu Gln Ser Arg Thr Cys Trp Leu Ala Ala Phe Arg Leu Phe

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<210> 126
<211> 1619
<212> DNA
<213> Homo sapiens
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<400>	126					
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gcccgcattt	ccctgtcctt	caccacgcgg	agctgcccac	cccctggagg	gtcttgggggt	240
tctggaagaa	gcagccccc	actaggcgga	aatgggaagg	ccaccatgca	gaatctcaac	300
gaccgcctgg	cctcctacct	ggagaaggtt	cgcgccttgg	aggaggccaa	catgaagctg	360
gaagaccgca	tcctgaaatg	gcaccagcag	agagatcctg	gcagtaagaa	agattatttc	420
cagtatgagg	aaaacatcac	acacctgcag	gagcagatag	tggatggtaa	gatgaccaat	480
gctcagatta	ttcttctcat	tgacaatgcc	aggatggcag	tggatgactt	caacctcaag	540
tatgaaaatg	aacactcctt	taagaaagac	ttggaaattg	aagtcgaggg	cctccgaagg	600
accttagaca	acctgaccat	tgtcacaaca	gacctagaac	aggaggtgga	aggaatgagg	660
aaagagctca	ttctcatgaa	ggagcaccat	gagcaggaaa	tggaggagca	tcatgtgcca	720
agtgacttca	atgtcaatgt	gaagtggtat	acaggtccca	gggaagatct	gattaaggtc	780
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acttggtata	aagaacagtc	tcgagccatg	tcccaggagg	cagccagctc	agccactgtg	900
cagagcagac	aaggtgacat	ccacgaactg	aagcgcacat	tccaggccct	ggagattgac	960
ctgcaggcac	agtacagcac	gaaatctgct	ttggaaaaca	tgttatccga	gaccagctct	1020
cggtaactct	gcaagctcca	ggacatgcaa	gagatcatct	cccactatga	ggaggaactg	1080
acgcagctac	gccacgaact	ggagcggcag	aacaatgaat	accaagtgtc	gctgggcatc	1140
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gggacaccgg	agaatacaga	gtcgaagcat	aaagtgtctg	caactccaa	gatcagggcc	1260
ataaccaggg	agaccatcaa	cggaaagatta	gttctttgtc	aagtgaatga	aatccaaaag	1320
cacgcatgag	accaatgaaa	gtttccgcct	gtttgtaaagt	ctattttccc	ccaagaaaaa	1380

137

tccttgacaca gacaccagtg agtgagttct aaaagataacc cttggaatta tcagactcag 1440  
 aaacttttat tttttttttt ctgtaacagt ctcaccagac ttctcataat gctcttaata 1500  
 tattgcactt ttctaataca agtgcgagtt tatgagggta aagctctact ttcctactgc 1560  
 agccttcaga ttctcatcat ttgcatcta tttgttagcc aataaaactc cgcactagc 1619

&lt;210&gt; 127

&lt;211&gt; 422

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 127

Met	Asn	Ser	Gly	His	Ser	Phe	Ser	Gln	Thr	Pro	Ser	Ala	Ser	Phe	His
1				5					10					15	
Gly	Ala	Gly	Gly	Gly	Trp	Gly	Arg	Pro	Arg	Ser	Phe	Pro	Arg	Ala	Pro
		20						25					30		
Thr	Val	His	Gly	Gly	Ala	Gly	Gly	Ala	Arg	Ile	Ser	Leu	Ser	Phe	Thr
		35					40					45			
Thr	Arg	Ser	Cys	Pro	Pro	Pro	Gly	Gly	Ser	Trp	Gly	Ser	Gly	Arg	Ser
	50					55					60				
Ser	Pro	Leu	Leu	Gly	Gly	Asn	Gly	Lys	Ala	Thr	Met	Gln	Asn	Leu	Asn
	65			70					75					80	
Asp	Arg	Leu	Ala	Ser	Tyr	Leu	Glu	Lys	Val	Arg	Ala	Leu	Glu	Glu	Ala
			85					90					95		
Asn	Met	Lys	Leu	Glu	Ser	Arg	Ile	Leu	Lys	Trp	His	Gln	Gln	Arg	Asp
		100						105					110		
Pro	Gly	Ser	Lys	Lys	Asp	Tyr	Ser	Gln	Tyr	Glu	Glu	Asn	Ile	Thr	His
		115					120					125			
Leu	Gln	Glu	Gln	Ile	Val	Asp	Gly	Lys	Met	Thr	Asn	Ala	Gln	Ile	Ile
	130					135					140				
Leu	Leu	Ile	Asp	Asn	Ala	Arg	Met	Ala	Val	Asp	Asp	Phe	Asn	Leu	Lys
	145			150					155					160	
Tyr	Glu	Asn	Glu	His	Ser	Phe	Lys	Lys	Asp	Leu	Glu	Ile	Glu	Val	Glu
			165						170					175	
Gly	Leu	Arg	Arg	Thr	Leu	Asp	Asn	Leu	Thr	Ile	Val	Thr	Thr	Asp	Leu
		180					185						190		
Glu	Gln	Glu	Val	Glu	Gly	Met	Arg	Lys	Glu	Leu	Ile	Leu	Met	Lys	Glu
		195				200						205			
His	His	Glu	Gln	Glu	Met	Glu	Glu	His	His	Val	Pro	Ser	Asp	Phe	Asn
	210				215						220				
Val	Asn	Val	Lys	Val	Asp	Thr	Gly	Pro	Arg	Glu	Asp	Leu	Ile	Lys	Val
	225				230					235				240	
Leu	Glu	Asp	Met	Arg	Gln	Glu	Tyr	Glu	Leu	Ile	Ile	Lys	Lys	Lys	His
			245					250					255		
Arg	Asp	Leu	Asp	Thr	Trp	Tyr	Lys	Glu	Gln	Ser	Ala	Ala	Met	Ser	Gln
		260					265						270		
Glu	Ala	Ala	Ser	Pro	Ala	Thr	Val	Gln	Ser	Arg	Gln	Gly	Asp	Ile	His
		275				280						285			
Glu	Leu	Lys	Arg	Thr	Phe	Gln	Ala	Leu	Glu	Ile	Asp	Leu	Gln	Ala	Gln
	290				295					300					
Tyr	Ser	Thr	Lys	Ser	Ala	Leu	Glu	Asn	Met	Leu	Ser	Glu	Thr	Gln	Ser
	305				310				315					320	
Arg	Tyr	Ser	Cys	Lys	Leu	Gln	Asp	Met	Gln	Glu	Ile	Ile	Ser	His	Tyr
			325					330					335		
Glu	Glu	Glu	Leu	Thr	Gln	Leu	Arg	His	Glu	Leu	Glu	Arg	Gln	Asn	Asn
			340				345						350		
Glu	Tyr	Gln	Val	Leu	Leu	Gly	Ile	Lys	Thr	His	Leu	Glu	Lys	Glu	Ile
		355				360						365			
Thr	Thr	Tyr	Arg	Arg	Leu	Leu	Glu	Gly	Glu	Ser	Glu	Gly	Thr	Arg	Glu

138

370	375	380
Glu Ser Lys Ser Ser Met Lys Val Ser Ala Thr	Pro Lys Ile Lys Ala	
385	390	395
Ile Thr Gln Glu Thr Ile Asn Gly Arg Leu Val	Leu Cys Gln Val Asn	400
	405	410
Glu Ile Gln Lys His Ala		415
	420	

&lt;210&gt; 128

&lt;211&gt; 1359

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 128

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aatgctttat tttctaaata tccagcctca agttcggttt tcgctaccgg agccttccca 180
gaacaaactt cttgtgcgtt tgcttccaac cccagcgcc cgggctatgg agcgggttcg 240
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&lt;210&gt; 129

&lt;211&gt; 217

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 129

Met Ser Ser Leu Tyr Tyr Ala Asn Ala Leu Phe Ser Lys Tyr Pro Ala	
1 5 10 15	
Ser Ser Ser Val Phe Ala Thr Gly Ala Phe Pro Glu Gln Thr Ser Cys	
20 25 30	
Ala Phe Ala Ser Asn Pro Gln Arg Pro Gly Tyr Gly Ala Gly Ser Gly	
35 40 45	
Ala Ser Phe Ala Gly Ser Met Gln Gly Leu Tyr Pro Gly Gly Gly Gly	
50 55 60	
Met Ala Gly Gln Ser Ala Ala Gly Val Tyr Ala Ala Gly Tyr Gly Leu	
65 70 75 80	
Glu Pro Ser Ser Phe Asn Met His Cys Ala Pro Phe Glu Gln Asn Leu	
85 90 95	
Ser Gly Val Cys Pro Gly Asp Ser Ala Lys Ala Ala Gly Ala Lys Glu	

[illegible]

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Val Pro Leu Leu Gly Leu Leu Arg Leu Gln Leu Arg Ala Ala Arg Gln
      20          25          30
Pro Gly Ala Met Arg Pro Gln Gly Pro Ala Ala Ser Pro Gln Arg Leu
      35          40          45
Arg Gly Leu Leu Leu Leu Leu Leu Leu Gln Leu Pro Ala Pro Ser Ser

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140

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65	70	75
Glu Val Val Asp Leu Tyr Asn Gly Met Cys	Leu Gln Gly Pro Ala Gly	80
	85	90
Val Pro Gly Arg Asp Gly Ser Pro Gly Ala Asn Gly Ile Pro Gly Thr		95
	100	105
Pro Gly Ile Pro Gly Arg Asp Gly Phe Lys Gly Glu Lys Gly Glu Cys		110
	115	120
Leu Arg Glu Ser Phe Glu Glu Ser Trp Thr Pro Asn Tyr Lys Gln Cys		125
	130	135
Ser Trp Ser Ser Leu Asn Tyr Gly Ile Asp Leu Gly Lys Ile Ala Glu		140
	145	150
Cys Thr Phe Thr Lys Met Arg Ser Asn Ser Ala Leu Arg Val Leu Phe		155
	160	165
Ser Gly Ser Leu Arg Leu Lys Cys Arg Asn Ala Cys Cys Gln Arg Trp		170
	175	180
Tyr Phe Thr Phe Asn Gly Ala Glu Cys Ser Gly Pro Leu Pro Ile Glu		185
	190	195
Ala Ile Ile Tyr Leu Asp Gln Gly Ser Pro Glu Met Asn Ser Thr Ile		200
	205	210
Asn Ile His Arg Thr Ser Ser Val Glu Gly Leu Cys Glu Gly Ile Gly		215
	220	225
Ala Gly Leu Val Asp Val Ala Ile Trp Val Gly Thr Cys Ser Asp Tyr		230
	235	240
Pro Lys Gly Asp Ala Ser Thr Gly Trp Asn Ser Val Ser Arg Ile Ile		245
	250	255
Ile Glu Glu Leu Pro Lys		260
	265	270
	275	

&lt;210&gt; 132

&lt;211&gt; 1177

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 132

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aaaattattt ccaacaaccw waaaaaaaaa aaaaagg 1177

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141

<210> 133  
 <211> 210  
 <212> PRT  
 <213> Homo sapiens

<400> 133  
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 Gln Tyr Asn Gly Met Cys Leu Gln Gly Pro Ala Gly Val Pro Gly Arg  
 20 25 30  
 Asp Gly Ser Pro Gly Ala Asn Gly Ile Pro Gly Thr Pro Gly Ile Pro  
 35 40 45  
 Gly Arg Asp Gly Phe Lys Gly Glu Lys Gly Glu Cys Leu Arg Glu Ser  
 50 55 60  
 Phe Glu Glu Ser Trp Thr Pro Asn Tyr Lys Gln Cys Ser Trp Ser Ser  
 65 70 75 80  
 Leu Asn Tyr Gly Ile Asp Leu Gly Lys Ile Ala Glu Cys Thr Phe Thr  
 85 90 95  
 Lys Met Arg Ser Asn Ser Ala Leu Arg Val Leu Phe Ser Gly Ser Leu  
 100 105 110  
 Arg Leu Lys Cys Arg Asn Ala Cys Cys Gln Arg Trp Tyr Phe Thr Phe  
 115 120 125  
 Asn Gly Ala Glu Cys Ser Gly Pro Leu Pro Ile Glu Ala Ile Ile Tyr  
 130 135 140  
 Leu Asp Gln Gly Ser Pro Glu Met Asn Ser Thr Ile Asn Ile His Arg  
 145 150 155 160  
 Thr Ser Ser Val Glu Gly Leu Cys Glu Gly Ile Gly Ala Gly Leu Val  
 165 170 175  
 Asp Val Ala Ile Trp Val Gly Thr Cys Ser Asp Tyr Pro Lys Gly Asp  
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 Ala Ser Thr Gly Trp Asn Ser Val Ser Arg Ile Ile Ile Glu Glu Leu  
 195 200 205  
 Pro Lys  
 210

<210> 134  
 <211> 1340  
 <212> DNA  
 <213> Homo sapiens

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 tgcccggcag ccgggagcca tgcgacccca gggcccccgc gcctccccgc agcgggtccg 240  
 cggcctcctg ctgctcctgc tgctgcagct gcccgcgccg tcgagcgccct ctgagatccc 300  
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142

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&lt;210&gt; 135

&lt;211&gt; 243

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 135

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Met Arg Pro Gln Gly Pro Ala Ala Ser Pro Gln Arg Leu Arg Gly Leu
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Leu Leu Leu Leu Leu Leu Gln Leu Pro Ala Pro Ser Ser Ala Ser Glu
 20          25          30
Ile Pro Lys Gly Lys Gln Lys Ala Gln Leu Arg Gln Arg Glu Val Val
 35          40          45
Asp Leu Tyr Asn Gly Met Cys Leu Gln Gly Pro Ala Gly Val Pro Gly
 50          55          60
Arg Asp Gly Ser Pro Gly Ala Asn Gly Ile Pro Gly Thr Pro Gly Ile
 65          70          75          80
Pro Gly Arg Asp Gly Phe Lys Gly Glu Lys Gly Glu Cys Leu Arg Glu
 85          90          95
Ser Phe Glu Glu Ser Trp Thr Pro Asn Tyr Lys Gln Cys Ser Trp Ser
100          105          110
Ser Leu Asn Tyr Gly Ile Asp Leu Gly Lys Ile Ala Glu Cys Thr Phe
115          120          125
Thr Lys Met Arg Ser Asn Ser Ala Leu Arg Val Leu Phe Ser Gly Ser
130          135          140
Leu Arg Leu Lys Cys Arg Asn Ala Cys Cys Gln Arg Trp Tyr Phe Thr
145          150          155          160
Phe Asn Gly Ala Glu Cys Ser Gly Pro Leu Pro Ile Glu Ala Ile Ile
165          170          175
Tyr Leu Asp Gln Gly Ser Pro Glu Met Asn Ser Thr Ile Asn Ile His
180          185          190
Arg Thr Ser Ser Val Glu Gly Leu Cys Glu Gly Ile Gly Ala Gly Leu
195          200          205
Val Asp Val Ala Ile Trp Val Gly Thr Cys Ser Asp Tyr Pro Lys Gly
210          215          220
Asp Ala Ser Thr Gly Trp Asn Ser Val Ser Arg Ile Ile Ile Glu Glu
225          230          235          240
Leu Pro Lys

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&lt;210&gt; 136

&lt;211&gt; 5519

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 136

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144

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&lt;210&gt; 137

&lt;211&gt; 765

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 137

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Asp Leu Asp Lys Thr Leu Gly Arg Gly His Phe Ala Val Val Lys Leu
  20          25          30
Ala Arg His Val Phe Thr Gly Glu Lys Val Ala Val Lys Val Ile Asp
  35          40          45
Lys Thr Lys Leu Asp Thr Leu Ala Thr Gly His Leu Phe Gln Glu Val
  50          55          60
Arg Cys Met Lys Leu Val Gln His Pro Asn Ile Val Arg Leu Tyr Glu
  65          70          75          80
Val Ile Asp Thr Gln Thr Lys Leu Tyr Leu Ile Leu Glu Leu Gly Asp
  85          90          95
Glu Gly Asp Met Phe Asp Tyr Ile Met Lys His Glu Glu Gly Leu Asn
  100         105         110
Glu Asp Leu Pro Lys Lys Tyr Phe Ala Gln Ile Val His Ala Ile Ser
  115         120         125
Tyr Cys His Lys Leu His Val His Arg Asp Leu Lys Pro Glu Asn
  130         135         140
Val Val Phe Phe Glu Lys Gln Gly Leu Val Lys Leu Thr Asp Phe Gly
  145         150         155         160
Phe Ser Asn Lys Phe Gln Pro Gly Lys Lys Leu Thr Thr Ser Cys Gly

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145

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Ala	Pro	Ala	Val	Asp	Ile	Trp	Ser	Leu	Gly	Val	Ile	Leu	Phe	Met	Leu
			195				200					205			
Val	Cys	Gly	Gln	Pro	Pro	Phe	Gln	Glu	Ala	Asn	Asp	Ser	Glu	Thr	Leu
	210					215					220				
Thr	Met	Ile	Met	Asp	Cys	Lys	Tyr	Thr	Val	Pro	Ser	His	Val	Ser	Lys
225				230						235					240
Glu	Cys	Lys	Asp	Leu	Ile	Thr	Arg	Met	Leu	Gln	Arg	Asp	Pro	Lys	Arg
			245						250					255	
Arg	Ala	Ser	Leu	Glu	Glu	Ile	Glu	Asn	His	Pro	Trp	Leu	Gln	Gly	Val
			260					265					270		
Asp	Pro	Ser	Pro	Ala	Thr	Lys	Tyr	Asn	Ile	Pro	Leu	Val	Ser	Tyr	Lys
			275				280					285			
Asn	Leu	Ser	Glu	Glu	Glu	His	Asn	Ser	Ile	Ile	Gln	Arg	Met	Val	Leu
	290					295					300				
Gly	Asp	Ile	Ala	Asp	Arg	Asp	Ala	Ile	Val	Glu	Ala	Leu	Glu	Thr	Asn
305					310					315					320
Arg	Tyr	Asn	His	Ile	Thr	Ala	Thr	Tyr	Phe	Leu	Leu	Ala	Glu	Arg	Ile
			325						330					335	
Leu	Arg	Glu	Lys	Gln	Glu	Lys	Glu	Ile	Gln	Thr	Arg	Ser	Ala	Ser	Pro
			340					345					350		
Ser	Asn	Ile	Lys	Ala	Gln	Phe	Arg	Gln	Ser	Trp	Pro	Thr	Lys	Ile	Asp
	355						360					365			
Val	Pro	Gln	Asp	Leu	Glu	Asp	Leu	Thr	Ala	Thr	Pro	Leu	Ser	His	
	370					375				380					
Ala	Thr	Val	Pro	Gln	Ser	Pro	Ala	Arg	Ala	Ala	Asp	Ser	Val	Leu	Asn
385					390					395					400
Gly	His	Arg	Ser	Lys	Gly	Leu	Cys	Asp	Ser	Ala	Lys	Lys	Asp	Asp	Leu
			405						410					415	
Pro	Glu	Leu	Ala	Gly	Pro	Ala	Leu	Ser	Thr	Val	Pro	Pro	Ala	Ser	Leu
			420					425					430		
Lys	Pro	Thr	Ala	Ser	Gly	Arg	Lys	Cys	Leu	Phe	Arg	Val	Glu	Glu	Asp
	435						440					445			
Glu	Glu	Glu	Asp	Glu	Glu	Asp	Lys	Lys	Pro	Met	Ser	Leu	Ser	Thr	Gln
	450					455					460				
Val	Val	Leu	Arg	Arg	Lys	Pro	Ser	Val	Thr	Asn	Arg	Leu	Thr	Ser	Arg
465					470					475					480
Lys	Ser	Ala	Pro	Val	Leu	Asn	Gln	Ile	Phe	Glu	Glu	Gly	Glu	Ser	Asp
			485						490					495	
Asp	Glu	Phe	Asp	Met	Asp	Glu	Asn	Leu	Pro	Pro	Lys	Leu	Ser	Arg	Leu
			500					505					510		
Lys	Met	Asn	Ile	Ala	Ser	Pro	Gly	Thr	Val	His	Lys	Arg	Tyr	His	Arg
	515						520					525			
Arg	Lys	Ser	Gln	Gly	Arg	Gly	Ser	Ser	Cys	Ser	Ser	Ser	Glu	Thr	Ser
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Asp	Asp	Asp	Ser	Glu	Ser	Arg	Arg	Arg	Leu	Asp	Lys	Asp	Ser	Gly	Phe
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Thr	Tyr	Ser	Trp	His	Arg	Arg	Asp	Ser	Ser	Glu	Gly	Pro	Pro	Gly	Ser
			565						570					575	
Glu	Gly	Asp	Gly	Gly	Gly	Gln	Ser	Lys	Pro	Ser	Asn	Ala	Ser	Gly	Gly
			580					585					590		
Val	Asp	Lys	Ala	Ser	Pro	Ser	Glu	Asn	Asn	Ala	Gly	Gly	Gly	Ser	Pro
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625					630					635				640	
Gly	Glu	Leu	Val	Glu	Ser	Leu	Lys	Leu	Met	Ser	Leu	Cys	Leu	Gly	Ser
				645					650					655	
Gln	Leu	His	Gly	Ser	Thr	Lys	Tyr	Ile	Ile	Asp	Pro	Gln	Asn	Gly	Leu
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Ser	Phe	Ser	Ser	Val	Lys	Val	Gln	Glu	Lys	Ser	Thr	Trp	Lys	Met	Cys
				675					680					685	
Ile	Ser	Ser	Thr	Gly	Asn	Ala	Gly	Gln	Val	Pro	Ala	Val	Gly	Gly	Ile
				690					695					700	
Lys	Phe	Phe	Ser	Asp	His	Met	Ala	Asp	Thr	Thr	Thr	Glu	Leu	Glu	Arg
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Ile	Lys	Ser	Lys	Asn	Leu	Lys	Asn	Asn	Val	Leu	Gln	Leu	Pro	Leu	Cys
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Glu	Lys	Thr	Ile	Ser	Val	Asn	Ile	Gln	Arg	Asn	Pro	Lys	Glu	Gly	Leu
				740					745					750	
Leu	Cys	Ala	Ser	Ser	Pro	Ala	Ser	Cys	Cys	His	Val	Ile			
		755						760				765			

&lt;210&gt; 138

&lt;211&gt; 2029

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 138

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Ser	Arg	Arg	Asp 20	Phe	Thr	Phe	Asp	Leu 25	Tyr	Arg	Ala	Leu	Ala 30	Ser	Ala
Ala	Pro	Ser 35	Gln	Asn	Ile	Phe	Phe 40	Ser	Pro	Val	Ser	Ile 45	Ser	Met	Ser
Leu 50	Ala	Met	Leu	Ser	Leu	Gly 55	Ala	Gly	Ser	Ser	Thr 60	Lys	Met	Gln	Ile
Leu 65	Glu	Gly	Leu	Gly	Leu	Asn 70	Leu	Gln	Lys	Ser	Ser 75	Glu	Lys	Glu	Leu 80
His	Arg	Gly	Phe 85	Gln	Gln	Leu	Leu	Gln	Glu 90	Leu	Asn	Gln	Pro	Arg 95	Asp
Gly	Phe	Gln 100	Leu	Ser	Leu	Gly	Asn 105	Ala	Leu	Phe	Thr	Asp 110	Leu	Val	Val
Asp	Leu	Gln 115	Asp	Thr	Phe	Val	Ser 120	Ala	Met	Lys	Thr 125	Leu	Tyr	Leu	Ala
Asp 130	Thr	Phe	Pro	Thr	Asn 135	Phe	Arg	Asp	Ser	Ala	Gly 140	Ala	Met	Lys	Gln
Ile 145	Asn	Asp	Tyr	Val 150	Ala	Lys	Gln	Thr	Lys 155	Gly	Lys	Ile	Val	Asp	Leu 160
Leu	Lys	Asn 165	Leu	Asp	Ser	Asn	Ala	Val 170	Val	Ile	Met	Val 175	Asn	Tyr	Ile 175
Phe	Phe	Lys 180	Ala	Lys	Trp	Glu	Thr 185	Ser	Phe	Asn	His	Lys 190	Gly	Thr	Gln
Glu	Gln	Asp 195	Phe	Tyr	Val	Thr	Ser 200	Glu	Thr	Val	Val 205	Arg	Val	Pro	Met
Met 210	Ser	Arg	Glu	Asp	Gln	Tyr 215	His	Tyr	Leu	Leu	Asp 220	Arg	Asn	Leu	Ser
Cys 225	Arg	Val	Val	Gly	Val	Pro 230	Tyr	Gln	Gly	Asn	Ala 235	Thr	Ala	Leu	Phe 240
Ile	Leu	Pro	Ser 245	Glu	Gly	Lys	Met	Gln	Gln 250	Val	Glu	Asn	Gly	Leu 255	Ser
Glu	Lys	Thr 260	Leu	Arg	Lys	Trp	Leu 265	Lys	Met	Phe	Lys	Lys 270	Arg	Gln	Leu
Glu	Leu	Tyr 275	Leu	Pro	Lys	Phe	Ser 280	Ile	Glu	Gly	Ser 285	Tyr	Gln	Leu	Glu
Lys 290	Val	Leu	Pro	Ser	Leu	Gly 295	Ile	Ser	Asn	Val	Phe 300	Thr	Ser	His	Ala
Asp 305	Leu	Ser	Gly	Ile	Ser 310	Asn	His	Ser	Asn	Ile 315	Gln	Val	Ser	Glu	Met 320
Val	His	Lys 325	Ala	Val	Val	Glu	Val	Asp	Glu 330	Ser	Gly	Thr	Arg	Ala	Ala
Ala	Ala	Thr 340	Gly	Thr	Ile	Phe	Thr 345	Phe	Arg	Ser	Ala 350	Arg	Leu	Asn	Ser
Gln	Arg	Leu 355	Val	Phe	Asn	Arg	Pro 360	Phe	Leu	Met	Phe 365	Ile	Val	Asp	Asn
Asn 370	Ile	Leu	Phe	Leu	Gly	Lys 375	Val	Asn	Arg	Pro					

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 <211> 2058  
 <212> DNA  
 <213> Homo sapiens

<400> 140  
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 gaacaatgga agtgacaaca agattgacat ggaatgatga aaatcatctg cgcaactgct 180  
 tggaaatggt tctttgagtc ttctctataa gtctagtgtt catggaggta gcattgaaga 240  
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 tatgattgta gcctttatgc ttggaaatta tattaattta cgtgaaagt ctacagagcc 360  
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 actcttaaat acagcaccaa aaattattga tgagcaactg gtgtgtcgtt tatcgaaaac 480  
 ggatattttc attatatgtc gagataataa aatttatcta gataaaatga taacaagaaa 540  
 cttgaaacta aggttttatg gccaccgtca gtatttgga tgtgaagttt ttcgagttga 600  
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 tattcttttg gtgggtccag ttgggtctgg aaagtccagt tttttcaatt cagtcaagtc 780  
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 cagtgcctgg taatgagcaa gcatacttgc cattactttt cttcccaact ctctccaaca 1980  
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 aaaccccatc tccactgc 2058

<210> 141  
 <211> 413  
 <212> PRT  
 <213> Homo sapiens

<400> 141  
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 Leu Arg Glu Ser Ser Thr Glu Pro Asn Asp Ser Leu Trp Phe Ser Leu  
 35 40 45  
 Gln Lys Lys Asn Asp Thr Thr Glu Ile Glu Thr Leu Leu Leu Asn Thr  
 50 55 60  
 Ala Pro Lys Ile Ile Asp Glu Gln Leu Val Cys Arg Leu Ser Lys Thr  
 65 70 75 80

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Asp Ile Phe Ile Ile Cys Arg Asp Asn Lys Ile Tyr Leu Asp Lys Met  
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 Ile Thr Arg Asn Leu Lys Leu Arg Phe Tyr Gly His Arg Gln Tyr Leu  
                             100                            105                            110  
 Glu Cys Glu Val Phe Arg Val Glu Gly Ile Lys Asp Asn Leu Asp Asp  
                             115                            120                            125  
 Ile Lys Arg Ile Ile Lys Ala Arg Glu His Arg Asn Arg Leu Leu Ala  
                             130                            135                            140  
 Asp Ile Arg Asp Tyr Arg Pro Tyr Ala Asp Leu Val Ser Glu Ile Arg  
                             145                            150                            155                            160  
 Ile Leu Leu Val Gly Pro Val Gly Ser Gly Lys Ser Ser Phe Phe Asn  
                             165                            170                            175  
 Ser Val Lys Ser Ile Phe His Gly His Val Thr Gly Gln Ala Val Val  
                             180                            185                            190  
 Gly Ser Asp Thr Thr Ser Ile Thr Glu Arg Tyr Arg Ile Tyr Ser Val  
                             195                            200                            205  
 Lys Asp Gly Lys Asn Gly Lys Ser Leu Pro Phe Met Leu Cys Asp Thr  
                             210                            215                            220  
 Met Gly Leu Asp Gly Ala Glu Gly Ala Gly Leu Cys Met Asp Asp Ile  
                             225                            230                            235                            240  
 Pro His Ile Leu Lys Gly Cys Met Pro Asp Arg Tyr Gln Phe Asn Ser  
                             245                            250                            255  
 Arg Lys Pro Ile Thr Pro Glu His Ser Thr Phe Ile Thr Ser Pro Ser  
                             260                            265                            270  
 Leu Lys Asp Arg Ile His Cys Val Ala Tyr Val Leu Asp Ile Asn Ser  
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 Ile Asp Asn Leu Tyr Ser Lys Met Leu Ala Lys Val Lys Gln Val His  
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 Lys Glu Val Leu Asn Cys Gly Ile Ala Tyr Val Ala Leu Leu Thr Lys  
                             305                            310                            315                            320  
 Val Asp Asp Cys Ser Glu Val Leu Gln Asp Asn Phe Leu Asn Met Ser  
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 Arg Ser Met Thr Ser Gln Ser Arg Val Met Asn Val His Lys Met Leu  
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 Gly Ile Pro Ile Ser Asn Ile Leu Met Val Gly Asn Tyr Ala Ser Asp  
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 Leu Glu Leu Asp Pro Met Lys Asp Ile Leu Ile Leu Ser Ala Leu Arg  
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 Gln Met Leu Arg Ala Ala Asp Asp Phe Leu Glu Asp Leu Pro Leu Glu  
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 Glu Thr Gly Ala Ile Glu Arg Ala Leu Gln Pro Cys Ile  
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&lt;210&gt; 142

&lt;211&gt; 1032

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 142

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 gctggacgctc cccacggcgg cgggtgcaggc gtccccctctg caagcgtag acttctttgg 180  
 gaatgggcca ccagttaact acaagacagg caatctatac ctgcgggggc ccctgaagaa 240  
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 cagtcggtg ccctacggaa acgcacagga acaaaatgtc agtggcaggt gggagttcaa 420  
 gtgccagctt ggagaagagg agtgcaaatt caacaagggt gaggcctgcg tgttgatga 480

150

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aactagttta at 1032

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&lt;210&gt; 143

&lt;211&gt; 303

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 143

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Met Asp Ser Arg His Thr Phe Ala Pro Ala Ala Met Thr Leu Ser Pro
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20      25      30
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35      40      45
Gly Pro Pro Val Asn Tyr Lys Thr Gly Asn Leu Tyr Leu Arg Gly Pro
50      55      60
Leu Lys Lys Ser Asn Ala Pro Leu Val Asn Val Thr Leu Tyr Tyr Glu
65      70      75      80
Ala Leu Cys Gly Gly Cys Arg Ala Phe Leu Ile Arg Glu Leu Phe Pro
85      90      95
Thr Trp Leu Leu Val Met Glu Ile Leu Asn Val Thr Ser Val Pro Tyr
100     105     110
Gly Asn Ala Gln Glu Gln Asn Val Ser Gly Arg Trp Glu Phe Lys Cys
115     120     125
Gln Leu Gly Glu Glu Glu Cys Lys Phe Asn Lys Val Glu Ala Cys Val
130     135     140
Leu Asp Glu Leu Asp Met Glu Leu Ala Phe Leu Thr Met Ser Gly Met
145     150     155     160
Ala Trp Lys Ser Leu Arg Thr Trp Arg Glu Val Cys His Tyr Ala Cys
165     170     175
Ser Ser Thr Pro Gln Gly Cys Arg Gln Asn Tyr His Gly Val Cys Asn
180     185     190
Gly Gly Pro Arg His Ala Ala His Ala Arg Gln Arg Pro Ala Asp Arg
195     200     205
Cys Ser Pro Ala Thr Ala Arg Val Cys Ala Leu Gly His Arg Gln Trp
210     215     220
Glu Thr Leu Gly Arg Ser Asp Pro Ala Pro Tyr Pro Cys Leu Pro Val
225     230     235     240
Val Pro Gly Gln Glu Ala Gly Cys Leu Pro Phe Leu Asn Gln Leu Pro
245     250     255
Pro Glu Cys Leu Leu Arg Val Leu Ala Gly Gly Leu Arg Arg Ala His
260     265     270
Gly Arg Arg Val Gly Thr Arg Leu Pro Ala Phe Phe Ser Asp Pro Asp
275     280     285
Pro Arg His Leu Leu Leu Thr Asn Trp Lys Ile Leu Cys Ile Pro
290     295     300

```

&lt;210&gt; 144

151

&lt;211&gt; 1356

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 144

```

ttctcccgca accttccctt cgtccctcc cgtcccccc agtccttagc ctccgactcc 60
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tctccccctc gccctctctt cggcccccc ctttcacgtt cactctgtct ctcccactat 240
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cctcgcccc cctcatcggg ctgaggaagc acagcagcat cttcaaacat gtacaaaatc 1320
gattggcttt aaacaccctt cacataccct ccccc 1356

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&lt;210&gt; 145

&lt;211&gt; 180

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 145

```

Met Gly Ile Pro Met Gly Lys Ser Met Leu Val Leu Leu Thr Phe Leu
 1           5           10           15
Ala Phe Ala Ser Cys Cys Ile Ala Ala Tyr Arg Pro Ser Glu Thr Leu
          20           25           30
Cys Gly Gly Glu Leu Val Asp Thr Leu Gln Phe Val Cys Gly Asp Arg
          35           40           45
Gly Phe Tyr Phe Ser Arg Pro Ala Ser Arg Val Ser Arg Arg Ser Arg
          50           55           60
Gly Ile Val Glu Glu Cys Cys Phe Arg Ser Cys Asp Leu Ala Leu Leu
          65           70           75           80
Glu Thr Tyr Cys Ala Thr Pro Ala Lys Ser Glu Arg Asp Val Ser Thr
          85           90           95
Pro Pro Thr Val Leu Pro Asp Asn Phe Pro Arg Tyr Pro Val Gly Lys
          100          105          110
Phe Phe Gln Tyr Asp Thr Trp Lys Gln Ser Thr Gln Arg Leu Arg Arg
          115          120          125
Gly Leu Pro Ala Leu Leu Arg Ala Arg Arg Gly His Val Leu Ala Lys
          130          135          140
Glu Leu Glu Ala Phe Arg Glu Ala Lys Arg His Arg Pro Leu Ile Ala
          145          150          155          160
Leu Pro Thr Gln Asp Pro Ala His Gly Gly Ala Pro Pro Glu Met Ala
          165          170          175
Ser Asn Arg Lys

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180

<210> 146  
<211> 3667  
<212> DNA  
<213> Homo sapiens

&lt;400&gt; 146

tatatcatgt	aagctagtc	cacctat	aattcact	tctttgt	ttgattt	60
atggctatta	ttgcaaca	caaacaa	ttgaata	tttgtga	agcactg	120
aaatatgagg	gaagttt	gtgttct	tttaaat	ttgcagt	atttgtg	180
caaatgtatg	catgtgaa	atacaga	taaaaaa	gatcatta	gattagg	240
taagggtgtag	tctgtacat	gaggaag	taagttg	cagaata	tggttag	300
tcgaagctag	cctggatt	aatcttg	ccaccac	ctagcta	aagcttag	360
aagcaactca	acggagg	cgaggag	cggtacc	gccgggg	ccgcggg	420
tcggggaaga	gacggat	gaacaag	tacatcg	acctgag	cgccgtc	480
gccgacgacc	tccggcag	ctttggg	aggaagc	ccctggc	acaggtc	540
ctgaagctcc	gctacgc	cgtggac	cccgacc	actgggc	ccgcgcc	600
gtagccctct	cggtgaa	ggaattg	gggaaat	tggaagt	ttactca	660
tctaaaaagc	taaggag	gaaaatt	attcgaa	tccctct	cctgcag	720
gaggtgttgg	atggact	ggctca	gggacag	agaatgt	acaagt	780
acagacacag	aaaccgc	tgtcaac	acatatg	caagaga	agcaaaa	840
gccatggaga	agctaag	gcatacg	gagaact	ccttcaa	ttcctac	900
ccggatgaag	aggtgag	cccttcg	cctcagc	cccagcg	ggaccac	960
tcccgggagc	aaggccac	ccctggg	acttctc	ccagaca	tgatttc	1020
ctgcggatcc	tggtccca	ccagttt	ggtgccat	tcggaaa	gggcttg	1080
ataaagaaca	tactaag	gacccag	cggttag	tccatag	agagaac	1140
ggagctgcag	agaagcc	caccatc	gccaccc	aggggac	tgaagca	1200
cgcatgattc	ttgaaat	gcagaaa	gcagatg	ccaaact	cgaagag	1260
cctctgaaaa	tcttggc	caatggc	gttgga	tgattgg	agaaggc	1320
aatttgaaga	aaattga	tgaaac	accaaga	caatctc	tttgcag	1380
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agtgtctaga	tagagatt	gaagaag	cgtgagg	ttgaaat	tatgctg	1500
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gaaaacttct	ttaaccc	agaaga	aagctga	cgcatat	agtgcct	1860
tccacagctg	gccgggt	tgcaaa	ggcaag	tgaacga	gcagaac	1920
accagtgcag	aagtcac	gcctcgt	caaacgc	atgaaa	ggaagt	1980
gtcagaatta	tcgggc	ctttgct	cagactg	agcgca	cagggaa	2040
gtacaacagg	tgaagc	ggagcag	taccctc	gagtcgc	acagcgc	2100
aagtgaggct	cccacag	ccagcaa	aacggat	tgtagcc	ccaacac	2160
acagaatgag	accaa	gccagcc	tcgggag	accaa	atctgag	2220
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atgcacaccc	tttttct	gcaaat	tctgtac	tgtgtac	ttagaa	2520
aagatgttaa	gatatgt	ctgtggg	cacaggg	ctgcagc	aatatat	2580
agaaataata	tatcaaat	ctcaact	tccaatt	aatcaat	taatttt	2640
ttctttttaa	agagaa	ggctttt	gacttta	aataa	ttgggag	2700
tcacggtgta	gagagg	ttgagg	ccgcaca	ttcacc	gggaa	2760
gtcggaagga	cactcac	agttctg	cacctgt	tgtcaac	agggata	2820
tctccttgaa	gaggaa	tgctact	catgcct	tagctca	accattt	2880
ctttgcttca	caggttt	actggtt	tgcata	tatata	tctgtct	2940

153

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tctgtttatc tctccctccc ctcccctccc cttcttctcc atctccattc ttttgaattt 3000
cctcatccct ccatctcaat cccgtatcta cgcaccccc cccccaggc aaagcagtgc 3060
tctgagatc acatcacaca aaaggaacaa aagcgaaaca cacaaaccag cctcaactta 3120
cacttggtta ctcaaaagaa caagagtcaa tggtagctgt cctagcgttt tggaagagga 3180
aaacaggaac ccaccaaacc aaccaatcaa ccaaacaag aaaaaattcc acaatgaaag 3240
aatgtatttt gtctttttgc attttggtgt ataagccatc aatattcagc aaaatgattc 3300
ctttctttaa aaaaaaaaaa tgtggaggaa agtagaaatt taccaagggtt gttggccag 3360
ggcgttaaat tcacagattt ttttaacgag aaaaacacac agaagaagct acctcagggtg 3420
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caagaacctt tatggccttc ttttgacaaa accttgaaaa tgtttattta aaaaaaaaaa 3660
aaaaaaa

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&lt;210&gt; 147

&lt;211&gt; 556

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 147

```

Met Met Asn Lys Leu Tyr Ile Gly Asn Leu Ser Pro Ala Val Thr Ala
1          5          10          15
Asp Asp Leu Arg Gln Leu Phe Gly Asp Arg Lys Leu Pro Leu Ala Gly
20          25          30
Gln Val Leu Leu Lys Ser Gly Tyr Ala Phe Val Asp Tyr Pro Asp Gln
35          40          45
Asn Trp Ala Ile Arg Ala Ile Glu Thr Leu Ser Gly Lys Val Glu Leu
50          55          60
His Gly Lys Ile Met Glu Val Asp Tyr Ser Val Ser Lys Lys Leu Arg
65          70          75          80
Ser Arg Lys Ile Gln Ile Arg Asn Ile Pro Pro His Leu Gln Trp Glu
85          90          95
Val Leu Asp Gly Leu Leu Ala Gln Tyr Gly Thr Val Glu Asn Val Glu
100         105         110
Gln Val Asn Thr Asp Thr Glu Thr Ala Val Val Asn Val Thr Tyr Ala
115         120         125
Thr Arg Glu Glu Ala Lys Ile Ala Met Glu Lys Leu Ser Gly His Gln
130         135         140
Phe Glu Asn Tyr Ser Phe Lys Ile Ser Tyr Ile Pro Asp Glu Glu Val
145         150         155         160
Ser Ser Pro Ser Pro Pro Gln Arg Ala Gln Arg Gly Asp His Ser Ser
165         170         175
Arg Glu Gln Gly His Ala Pro Gly Gly Thr Ser Gln Ala Arg Gln Ile
180         185         190
Asp Phe Pro Leu Arg Ile Leu Val Pro Thr Gln Phe Val Gly Ala Ile
195         200         205
Ile Gly Lys Glu Gly Leu Thr Ile Lys Asn Ile Thr Lys Gln Thr Gln
210         215         220
Ser Arg Val Asp Ile His Arg Lys Glu Asn Ser Gly Ala Ala Glu Lys
225         230         235         240
Pro Val Thr Ile His Ala Thr Pro Glu Gly Thr Ser Glu Ala Cys Arg
245         250         255
Met Ile Leu Glu Ile Met Gln Lys Glu Ala Asp Glu Thr Lys Leu Ala
260         265         270
Glu Glu Ile Pro Leu Lys Ile Leu Ala His Asn Gly Leu Val Gly Arg
275         280         285
Leu Ile Gly Lys Glu Gly Arg Asn Leu Lys Lys Ile Glu His Glu Thr
290         295         300

```

154

Gly Thr Lys Ile Thr Ile Ser Ser Leu Gln Asp Leu Ser Ile Tyr Asn  
 305 310 315 320  
 Pro Glu Arg Thr Ile Thr Val Lys Gly Thr Val Glu Ala Cys Ala Ser  
 325 330 335  
 Ala Glu Ile Glu Ile Met Lys Lys Leu Arg Glu Ala Phe Glu Asn Asp  
 340 345 350  
 Met Leu Ala Val Asn Thr His Ser Gly Tyr Phe Ser Ser Leu Tyr Pro  
 355 360 365  
 His His Gln Phe Gly Pro Phe Pro His His His Ser Tyr Pro Glu Gln  
 370 375 380  
 Glu Ile Val Asn Leu Phe Ile Pro Thr Gln Ala Val Gly Ala Ile Ile  
 385 390 395 400  
 Gly Lys Lys Gly Ala His Ile Lys Gln Leu Ala Arg Phe Ala Gly Ala  
 405 410 415  
 Ser Ile Lys Ile Ala Pro Ala Glu Gly Pro Asp Val Ser Glu Arg Met  
 420 425 430  
 Val Ile Ile Thr Gly Pro Pro Glu Ala Gln Phe Lys Ala Gln Gly Arg  
 435 440 445  
 Ile Phe Gly Lys Leu Lys Glu Glu Asn Phe Phe Asn Pro Lys Glu Glu  
 450 455 460  
 Val Lys Leu Glu Ala His Ile Arg Val Pro Ser Ser Thr Ala Gly Arg  
 465 470 475 480  
 Val Ile Gly Lys Gly Gly Lys Thr Val Asn Glu Leu Gln Asn Leu Thr  
 485 490 495  
 Ser Ala Glu Val Ile Val Pro Arg Asp Gln Thr Pro Asp Glu Asn Glu  
 500 505 510  
 Glu Val Ile Val Arg Ile Ile Gly His Phe Phe Ala Ser Gln Thr Ala  
 515 520 525  
 Gln Arg Lys Ile Arg Glu Ile Val Gln Gln Val Lys Gln Gln Glu Gln  
 530 535 540  
 Lys Tyr Pro Gln Gly Val Ala Ser Gln Arg Ser Lys  
 545 550 555

&lt;210&gt; 148

&lt;211&gt; 1475

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 148

cccagaggag cagactacaa gaatggcaca cgctatggaa aactcctgga caatcagtaa 60  
 agagtaccat attgatgaag aagtgggctt tgctctgcca aatccacagg aaaatctacc 120  
 tgatttttat aatgactgga tgttcattgc taaacatctg cctgatctca tagagtctgg 180  
 ccagcttcga gaaagagttg agaagttaaa catgctcagc attgatcatc tcacagacca 240  
 caagtcacag cgccttgacac gtctagttct gggatgcatc accatggcat atgtgtgggg 300  
 caaaggatcat ggagatgtcc gtaaggctt gccaaagaaat attgctgttc cttactgcca 360  
 actctccaag aaactggaac tgcctcctat tttggtttat gcagactgtg tcttggcaaa 420  
 ctggaagaaa aaggatccta ataagccct gacttatgag aacatggacg tttgttctc 480  
 atttcgtgat ggagactgca gtaaaggatt cttcctggtc tctctattgg tggaaatagc 540  
 agctgcttct gcaatcaaag taattcctac tgtattcaag gcaatgcaaa tgcaagaacg 600  
 ggacactttg ctaaaggcgc tgttggaat agcttcttgc ttggagaaag cccttcaagt 660  
 gtttcaccaa atccacgac atgtgaaccc aaaagcattt ttcagtgttc ttcgcatata 720  
 tttgtctggc tggaaaggca acccccagct atcagacggg ctggtgtatg aagggttctg 780  
 ggaagaccca aaggagttt cagggggcag tgcaggccaa agcagcgtct ttcagtgtt 840  
 tgacgtctcg ctgggcatcc agcagactgc tgggtggagga catgctgctc agttcctcca 900  
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155

```

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tacaactgag aaatcccttt tgaaggaagg ttaatgtaac ccaacaagag cacattttat 1260
catagcagag acatctgtat gcattcctgt cattacccat tgtaacagag ccacaaacta 1320
atactatgca atgttttacc aataatgcaa tacaaaagac ctcaaaatac ctgtgcattt 1380
cttgtaggaa aacaacaaaa ggtaattatg tgtaattata ctagaagttt tgtaatctgt 1440
atcttatcat tggaataaaa tgacattcaa taaat 1475

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&lt;210&gt; 149

&lt;211&gt; 403

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 149

```

Met Ala His Ala Met Glu Asn Ser Trp Thr Ile Ser Lys Glu Tyr His
 1          5          10          15
Ile Asp Glu Glu Val Gly Phe Ala Leu Pro Asn Pro Gln Glu Asn Leu
      20          25          30
Pro Asp Phe Tyr Asn Asp Trp Met Phe Ile Ala Lys His Leu Pro Asp
      35          40          45
Leu Ile Glu Ser Gly Gln Leu Arg Glu Arg Val Glu Lys Leu Asn Met
      50          55          60
Leu Ser Ile Asp His Leu Thr Asp His Lys Ser Gln Arg Leu Ala Arg
      65          70          75          80
Leu Val Leu Gly Cys Ile Thr Met Ala Tyr Val Trp Gly Lys Gly His
      85          90          95
Gly Asp Val Arg Lys Val Leu Pro Arg Asn Ile Ala Val Pro Tyr Cys
      100          105          110
Gln Leu Ser Lys Lys Leu Glu Leu Pro Pro Ile Leu Val Tyr Ala Asp
      115          120          125
Cys Val Leu Ala Asn Trp Lys Lys Lys Asp Pro Asn Lys Pro Leu Thr
      130          135          140
Tyr Glu Asn Met Asp Val Leu Phe Ser Phe Arg Asp Gly Asp Cys Ser
      145          150          155          160
Lys Gly Phe Phe Leu Val Ser Leu Leu Val Glu Ile Ala Ala Ala Ser
      165          170          175
Ala Ile Lys Val Ile Pro Thr Val Phe Lys Ala Met Gln Met Gln Glu
      180          185          190
Arg Asp Thr Leu Leu Lys Ala Leu Leu Glu Ile Ala Ser Cys Leu Glu
      195          200          205
Lys Ala Leu Gln Val Phe His Gln Ile His Asp His Val Asn Pro Lys
      210          215          220
Ala Phe Phe Ser Val Leu Arg Ile Tyr Leu Ser Gly Trp Lys Gly Asn
      225          230          235          240
Pro Gln Leu Ser Asp Gly Leu Val Tyr Glu Gly Phe Trp Glu Asp Pro
      245          250          255
Lys Glu Phe Ala Gly Gly Ser Ala Gly Gln Ser Ser Val Phe Gln Cys
      260          265          270
Phe Asp Val Leu Leu Gly Ile Gln Gln Thr Ala Gly Gly Gly His Ala
      275          280          285
Ala Gln Phe Leu Gln Asp Met Arg Arg Tyr Met Pro Pro Ala His Arg
      290          295          300
Asn Phe Leu Cys Ser Leu Glu Ser Asn Pro Ser Val Arg Glu Phe Val
      305          310          315          320
Leu Ser Lys Gly Asp Ala Gly Leu Arg Glu Ala Tyr Asp Ala Cys Val
      325          330          335
Lys Ala Leu Val Ser Leu Arg Ser Tyr His Leu Gln Ile Val Thr Lys
      340          345          350

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156

Tyr Ile Leu Ile Pro Ala Ser Gln Gln Pro Lys Glu Asn Lys Thr Ser  
           355                                  360                                  365  
 Glu Asp Pro Ser Lys Leu Glu Ala Lys Gly Thr Gly Gly Thr Asp Leu  
           370                                  375                                  380  
 Met Asn Phe Leu Lys Thr Val Arg Ser Thr Thr Glu Lys Ser Leu Leu  
 385                                  390                                  395                                  400  
 Lys Glu Gly

&lt;210&gt; 150

&lt;211&gt; 2129

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 150

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cagactgcca taagatggcg tccgtggcgg ctgcacgagc agttcctgtg ggcagtgggc 60
tcaggggcct gcaacggacc ctacctcttg tagtgattct cggggccacg ggcacssgmr 120
aatccacgct ggcgttgacg ctaggccagc ggctcggcgg tgagatcgtc agcgctgact 180
ccatgcaggc ctatgaaggc ctagacatca tcaccaacaa ggtttctgcc caagagcaga 240
gaatctgccc gcaccacatg atcagctttg tggatcctct tgtgaccaat tacacagtgg 300
tggacttcag aaatagagca actgctctga ttgaagatat atttgccga gacaaaattc 360
ctattgttgt gggaggaacc aattattaca ttgaatctct gctctggaaa gttcttgta 420
ataccaagcc ccaggagatg ggcactgaga aagtgattga cggaaaagtg gagcttgaaa 480
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gaatctctca tagtgaattt ctccatcgtc aacatacgga agaaggtggt ggtccccttg 660
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aatttaaaaa aaaaaaaaaa aaaaaaaaaa

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&lt;210&gt; 151

&lt;211&gt; 465

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

157

&lt;400&gt; 151

```

Met Ala Ser Val Ala Ala Ala Arg Ala Val Pro Val Gly Ser Gly Leu
 1          5          10          15
Arg Gly Leu Gln Arg Thr Leu Pro Leu Val Val Ile Leu Gly Ala Thr
 20          25          30
Gly Thr Ser Thr Leu Ala Leu Gln Leu Gly Gln Arg Leu Gly Gly Glu
 35          40          45
Ile Val Ser Ala Asp Ser Met Gln Val Tyr Glu Gly Leu Asp Ile Ile
 50          55          60
Thr Asn Lys Val Ser Ala Gln Glu Gln Arg Ile Cys Arg His His Met
 65          70          75          80
Ile Ser Phe Val Asp Pro Leu Val Thr Asn Tyr Thr Val Val Asp Phe
 85          90          95
Arg Asn Arg Ala Thr Ala Leu Ile Glu Asp Ile Phe Ala Arg Asp Lys
100          105          110
Ile Pro Ile Val Val Gly Gly Thr Asn Tyr Tyr Ile Glu Ser Leu Leu
115          120          125
Trp Lys Val Leu Val Asn Thr Lys Pro Gln Glu Met Gly Thr Glu Lys
130          135          140
Val Ile Asp Arg Lys Val Glu Leu Glu Lys Glu Asp Gly Leu Val Leu
145          150          155          160
His Lys Arg Leu Ser Gln Val Asp Pro Glu Met Ala Ala Lys Leu His
165          170          175
Pro His Asp Lys Arg Lys Val Ala Arg Ser Leu Gln Val Phe Glu Glu
180          185          190
Thr Gly Ile Ser His Ser Glu Phe Leu His Arg Gln His Thr Glu Glu
195          200          205
Gly Gly Gly Pro Leu Gly Gly Pro Leu Lys Phe Ser Asn Pro Cys Ile
210          215          220
Leu Trp Leu His Ala Asp Gln Ala Val Leu Asp Glu Arg Leu Asp Lys
225          230          235          240
Arg Val Asp Asp Met Leu Ala Ala Gly Leu Leu Glu Glu Leu Arg Asp
245          250          255
Phe His Arg Arg Tyr Asn Gln Lys Asn Val Ser Glu Asn Ser Gln Asp
260          265          270
Tyr Gln His Gly Ile Phe Gln Ser Ile Gly Phe Lys Glu Phe His Glu
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Tyr Leu Ile Thr Glu Gly Lys Cys Thr Leu Glu Thr Ser Asn Gln Leu
290          295          300
Leu Lys Lys Gly Ile Glu Ala Leu Lys Gln Val Thr Lys Arg Tyr Ala
305          310          315          320
Arg Lys Gln Asn Arg Trp Val Lys Asn Arg Phe Leu Ser Arg Pro Gly
325          330          335
Pro Ile Val Pro Pro Val Tyr Gly Leu Glu Val Ser Asp Val Ser Lys
340          345          350
Trp Glu Glu Ser Val Leu Glu Pro Ala Leu Glu Ile Val Gln Ser Phe
355          360          365
Ile Gln Gly His Lys Pro Thr Ala Thr Pro Ile Lys Met Pro Tyr Asn
370          375          380
Glu Ala Glu Asn Lys Arg Ser Tyr His Leu Cys Asp Leu Cys Asp Arg
385          390          395          400
Ile Ile Ile Gly Asp Arg Glu Trp Ala Ala His Ile Lys Ser Lys Ser
405          410          415
His Leu Asn Gln Leu Lys Lys Arg Arg Leu Asp Ser Asp Ala Val
420          425          430
Asn Thr Ile Glu Ser Gln Ser Val Ser Pro Asp His Asn Lys Glu Pro
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158

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<212> DNA  
<213> Homo sapiens

<400> 152

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<400> 153

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159

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 Gly Glu Ile Val Ser Ala Asp Ser Met Gln Val Tyr Glu Gly Leu Asp  
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 Ile Ile Thr Asn Lys Val Ser Ala Gln Glu Gln Arg Ile Cys Arg His  
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 Asp Lys Ile Pro Ile Val Val Gly Thr Asn Tyr Tyr Ile Glu Ser  
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 Cys Ile Leu Trp Leu His Ala Asp Gln Ala Val Leu Asp Glu Arg Leu  
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160

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&lt;210&gt; 155

&lt;211&gt; 1066

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 155

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Gly Ser Leu Phe Gly Tyr Ser Val Ala Leu His Arg Gln Thr Glu Arg
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Gln Gln Arg Tyr Leu Leu Ala Gly Ala Pro Arg Glu Leu Ala Val
 65          70          75          80
Pro Asp Gly Tyr Thr Asn Arg Thr Gly Ala Val Tyr Leu Cys Pro Leu
 85          90          95
Thr Ala His Lys Asp Asp Cys Glu Arg Met Asn Ile Thr Val Lys Asn
100          105          110
Asp Pro Gly His His Ile Ile Glu Asp Met Trp Leu Gly Val Thr Val
115          120          125
Ala Ser Gln Gly Pro Ala Gly Arg Val Leu Val Cys Ala His Arg Tyr
130          135          140
Thr Gln Val Leu Trp Ser Gly Ser Glu Asp Gln Arg Arg Met Val Gly
145          150          155          160
Lys Cys Tyr Val Arg Gly Asn Asp Leu Glu Leu Asp Ser Ser Asp Asp
165          170          175
Trp Gln Thr Tyr His Asn Glu Met Cys Asn Ser Asn Thr Asp Tyr Leu
180          185          190
Glu Thr Gly Met Cys Gln Leu Gly Thr Ser Gly Gly Phe Thr Gln Asn
195          200          205
Thr Val Tyr Phe Gly Ala Pro Gly Ala Tyr Asn Trp Lys Gly Asn Ser
210          215          220

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162

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Pro	Arg	His	Arg	His	Met	Gly	Ala	Val	Phe	Leu	Leu	Ser	Gln	Glu	Ala
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Ala	Tyr	Phe	Gly	Ser	Ala	Ile	Ala	Leu	Ala	Asp	Leu	Asn	Asn	Asp	Gly
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Trp	Gln	Asp	Leu	Leu	Val	Gly	Ala	Pro	Tyr	Tyr	Phe	Glu	Arg	Lys	Glu
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Glu	Val	Gly	Gly	Ala	Ile	Tyr	Val	Phe	Met	Asn	Gln	Ala	Gly	Thr	Ser
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Phe	Pro	Ala	His	Pro	Ser	Leu	Leu	Leu	His	Gly	Pro	Ser	Gly	Ser	Ala
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Phe	Gly	Leu	Ser	Val	Ala	Ser	Ile	Gly	Asp	Ile	Asn	Gln	Asp	Gly	Phe
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Gln	Asp	Ile	Ala	Val	Gly	Ala	Pro	Phe	Glu	Gly	Leu	Gly	Lys	Val	Tyr
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Ile	Tyr	His	Ser	Ser	Ser	Lys	Gly	Leu	Leu	Arg	Gln	Pro	Gln	Gln	Val
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Ile	His	Gly	Glu	Lys	Leu	Gly	Leu	Pro	Gly	Leu	Ala	Thr	Phe	Gly	Tyr
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Ser	Leu	Ser	Gly	Gln	Met	Asp	Val	Asp	Glu	Asn	Phe	Tyr	Pro	Asp	Leu
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Asp	Pro	Ala	Leu	Cys	Thr	Ala	Thr	Ser	Cys	Val	Gln	Val	Glu	Leu	Cys
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Phe	Ala	Tyr	Asn	Gln	Ser	Ala	Gly	Asn	Pro	Asn	Tyr	Arg	Arg	Asn	Ile
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Thr	Leu	Ala	Tyr	Thr	Leu	Glu	Ala	Asp	Arg	Asp	Arg	Arg	Pro	Pro	Arg
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Leu	Arg	Phe	Ala	Gly	Ser	Glu	Ser	Ala	Val	Phe	His	Gly	Phe	Phe	Ser
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Met	Pro	Glu	Met	Arg	Cys	Gln	Lys	Leu	Glu	Leu	Leu	Leu	Met	Asp	Asn
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Leu	Arg	Asp	Lys	Leu	Arg	Pro	Ile	Ile	Ile	Ser	Met	Asn	Tyr	Ser	Leu
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Arg	Leu	Gln	Tyr	Ser	Arg	Asp	Val	Arg	Lys	Leu	Leu	Leu	Ser	Ile	Asn
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163

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 785 790 795 800  
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 835 840 845  
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 Lys Ser Glu Thr Val Leu Thr Cys Ala Thr Gly Arg Ala His Cys Val  
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&lt;211&gt; 8747

&lt;212&gt; DNA

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&lt;400&gt; 156

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&lt;210&gt; 157

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169

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&lt;210&gt; 159

&lt;211&gt; 624

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 159

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 20          25          30
Ser Glu Lys Thr His Pro Lys Asp Tyr Pro Arg Arg Ala Asn His Trp
 35          40          45
Ser Ala Ile Ile Gly Gly Ser His Ser Lys Asn Tyr Val Leu Trp Glu
 50          55          60
Tyr Gly Gly Tyr Ala Ser Glu Gly Val Lys Gln Val Ala Glu Leu Gly
 65          70          75          80
Ser Pro Val Lys Met Glu Glu Glu Ile Arg Gln Gln Ser Asp Glu Val
 85          90          95
Leu Thr Val Ile Lys Ala Lys Ala Gln Trp Pro Ala Trp Gln Pro Leu
100          105          110
Asn Val Arg Ala Ala Pro Ser Ala Glu Phe Ser Val Asp Arg Thr Arg
115          120          125
His Leu Met Ser Phe Leu Thr Met Met Gly Pro Ser Pro Asp Trp Asn

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170

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Gly Val Thr Tyr Glu	Ser Pro Asn Lys Pro Thr	Ile Pro Gln Glu Lys
	180	185
Ile Arg Pro Leu Thr	Ser Leu Asp His Pro Gln	Ser Pro Phe Tyr Asp
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Pro Glu Gly Gly Ser	Ile Thr Gln Val Ala Arg	Val Val Ile Glu Arg
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225	230	235
Asp Ile Val Ala Asp	Leu Ala Pro Glu Glu Lys	Asp Glu Asp Asp Thr
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Pro Glu Thr Cys Ile	Tyr Ser Asn Trp Ser Pro	Trp Ser Ala Cys Ser
	260	265
Ser Ser Thr Cys Asp	Lys Gly Lys Arg Met Arg	Gln Arg Met Leu Lys
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Ala Gln Leu Asp Leu	Ser Val Pro Cys Pro Asp	Thr Gln Asp Phe Gln
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Pro Cys Met Gly Pro	Gly Cys Ser Asp Glu Asp	Gly Ser Thr Cys Thr
305	310	315
Met Ser Glu Trp Ile	Thr Trp Ser Pro Cys Ser	Ile Ser Cys Gly Met
	325	330
Gly Met Arg Ser Arg	Glu Arg Tyr Val Lys Gln	Phe Pro Glu Asp Gly
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Ser Val Cys Thr Leu	Pro Thr Glu Glu Thr Glu	Lys Cys Thr Val Asn
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Glu Glu Cys Ser Pro	Ser Ser Cys Leu Met Thr	Glu Trp Gly Glu Trp
	370	375
Asp Glu Cys Ser Ala	Thr Cys Gly Met Gly Met	Lys Lys Arg His Arg
385	390	395
Met Ile Lys Met Asn	Pro Ala Asp Gly Ser Met	Cys Lys Ala Glu Thr
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	450	455
Gly Asp Cys Asn Glu	Asp Leu Glu Gln Val Glu	Lys Cys Met Leu Pro
465	470	475
Glu Cys Pro Ile Asp	Cys Glu Leu Thr Glu Trp	Ser Gln Trp Ser Glu
	485	490
Cys Asn Lys Ser Cys	Gly Lys Gly His Val Ile	Arg Thr Arg Met Ile
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Gln Met Glu Pro Gln	Phe Gly Gly Ala Pro Cys	Pro Glu Thr Val Gln
	515	520
Arg Lys Lys Cys Arg	Ile Arg Lys Cys Leu Arg	Asn Pro Ser Ile Gln
	530	535
Lys Leu Arg Trp Arg	Glu Ala Arg Glu Ser Arg	Arg Ser Glu Gln Leu
545	550	555
Lys Glu Glu Ser Glu	Gly Glu Gln Phe Pro Gly	Cys Arg Met Arg Pro
	565	570
Trp Thr Ala Trp Ser	Glu Cys Thr Lys Leu Cys	Gly Gly Gly Ile Gln
	580	585
Glu Arg Tyr Met Thr	Val Lys Lys Arg Phe Lys	Ser Ser Gln Phe Thr

171

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 <211> 3408  
 <212> DNA  
 <213> Homo sapiens

<400> 160  
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 ctctctggag agttcgagtt tcccgctacc gaaacagtag ctggatgtga gctcccagac 180  
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 gcttgacagt gaggcctggc ctgggggtgct ggactcagag agggaccggc tgatccttat 360  
 caacgagaag gaggagctgc tgaaggagat gcgcttcac agcccccgca agtggaccca 420  
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&lt;210&gt; 161

&lt;211&gt; 888

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 161

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20     25     30
Ser Asp Leu Trp Ser Ser Ser Ser Ser Leu Glu Ser Ser Ser Phe Pro
35     40     45
Leu Pro Lys Gln Tyr Leu Asp Val Ser Ser Gln Thr Asp Ile Ser Gly
50     55     60
Ser Phe Gly Ile Asn Ser Asn Asn Gln Leu Ala Glu Lys Val Arg Leu
65     70     75     80
Arg Leu Arg Tyr Glu Glu Ala Lys Arg Arg Ile Ala Asn Leu Lys Ile
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Gln Leu Ala Lys Leu Asp Ser Glu Ala Trp Pro Gly Val Leu Asp Ser
100    105    110
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115    120    125
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130    135    140
Gln Leu Glu Met Ala Arg Lys Arg Leu Glu Lys Asp Leu Gln Ala Ala
145    150    155    160
Arg Asp Thr Gln Ser Lys Ala Leu Thr Glu Arg Leu Lys Leu Asn Ser
165    170    175
Lys Arg Asn Gln Leu Val Arg Glu Leu Glu Glu Ala Thr Arg Gln Val
180    185    190
Ala Thr Leu His Ser Gln Leu Lys Ser Leu Ser Ser Ser Met Gln Ser
195    200    205
Leu Ser Ser Gly Ser Ser Pro Gly Ser Leu Thr Ser Ser Arg Gly Ser
210    215    220
Leu Val Ala Ser Ser Leu Asp Ser Ser Thr Ser Ala Ser Phe Thr Asp
225    230    235    240
Leu Tyr Tyr Asp Pro Phe Glu Gln Leu Asp Ser Glu Leu Gln Ser Lys
245    250    255
Val Glu Phe Leu Leu Leu Glu Gly Ala Thr Gly Phe Arg Pro Ser Gly
260    265    270
Cys Ile Thr Thr Ile His Glu Asp Glu Val Ala Lys Thr Gln Lys Ala
275    280    285
Glu Gly Gly Gly Arg Leu Gln Ala Leu Arg Ser Leu Ser Gly Thr Pro
290    295    300
Lys Ser Met Thr Ser Leu Ser Pro Arg Ser Ser Leu Ser Ser Pro Ser
305    310    315    320
Pro Pro Cys Ser Pro Leu Met Ala Asp Pro Leu Leu Ala Gly Asp Ala

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Glu	Pro	Gly	Thr	Glu	Gly	Lys	Gln	Leu	Gly	Gln	Ala	Val	Asn	Thr	Ala	
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Gln	Gly	Cys	Gly	Leu	Lys	Val	Ala	Cys	Val	Ser	Ala	Ala	Val	Ser	Asp	
385					390					395					400	
Glu	Ser	Val	Ala	Gly	Asp	Ser	Gly	Val	Tyr	Glu	Ala	Ser	Val	Gln	Arg	
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Leu	Gly	Ala	Ser	Glu	Ala	Ala	Ala	Phe	Asp	Ser	Asp	Glu	Ser	Glu	Ala	
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Val	Gly	Ala	Thr	Arg	Ile	Gln	Ile	Ala	Leu	Lys	Tyr	Asp	Glu	Lys	Asn	
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		450				455					460					
Leu	Gln	Gln	Gln	Asp	Gln	Lys	Val	Asn	Ile	Arg	Val	Ala	Val	Leu	Pro	
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Cys	Ser	Glu	Ser	Thr	Thr	Cys	Leu	Phe	Arg	Thr	Arg	Pro	Leu	Asp	Ala	
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Ser	Asp	Thr	Leu	Val	Phe	Asn	Glu	Val	Phe	Trp	Val	Ser	Met	Ser	Tyr	
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Pro	Ala	Leu	His	Gln	Lys	Thr	Leu	Arg	Val	Asp	Val	Cys	Thr	Thr	Asp	
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Ser	Tyr	Lys	Tyr	Leu	Lys	Lys	Gln	Ser	Arg	Glu	Leu	Lys	Pro	Val	Gly	
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Val	Met	Ala	Pro	Ala	Ser	Gly	Pro	Ala	Ser	Thr	Asp	Ala	Val	Ser	Ala	
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174

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Arg	Leu	Leu	Leu	Arg	Met	Leu	Glu	Lys	Arg	Met	Asp	Arg	Ala	Glu	His
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Lys	Gly	Glu	Leu	Gln	Thr	Asp	Lys	Met	Met	Arg	Ala	Ala	Ala	Lys	Asp
			835					840					845		
Val	His	Arg	Leu	Arg	Gly	Gln	Ser	Cys	Lys	Glu	Pro	Pro	Glu	Val	Gln
			850				855					860			
Ser	Phe	Arg	Glu	Lys	Met	Ala	Phe	Phe	Thr	Arg	Pro	Arg	Met	Asn	Ile
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Pro	Ala	Leu	Ser	Ala	Asp	Asp	Val								
							885								

&lt;210&gt; 162

&lt;211&gt; 5794

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 162

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176

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178

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&lt;210&gt; 165

&lt;211&gt; 421

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 165

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Asn Arg Gly Cys Glu Ala Met Val Cys Asp Asn Leu Asn Leu Pro Phe
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Arg Asp Glu Gly Phe Asp Ala Ile Ile Ser Ile Gly Val Ile His His
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85           90           95
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Cys Ser Glu Cys Ser Cys Ser Val Cys Phe Lys Glu Gln Gly Gly Ser
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Phe Ala Asn Ile Ser Lys Glu Gly Glu Glu Glu Tyr Gly Phe Tyr Ser
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179

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&lt;210&gt; 166

&lt;211&gt; 1454

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 166

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&lt;210&gt; 167

&lt;211&gt; 276

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 167

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 Cys Gln Ser Asp Ser Gly Gly Pro Leu Val Cys Asp Glu Thr Leu Gln  
 225 230 235 240  
 Gly Ile Leu Ser Trp Gly Val Tyr Pro Cys Gly Ser Ala Gln His Pro  
 245 250 255  
 Ala Val Tyr Thr Gln Ile Cys Lys Tyr Met Ser Trp Ile Asn Lys Val  
 260 265 270  
 Ile Arg Ser Asn  
 275

&lt;210&gt; 168

&lt;211&gt; 1506

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 168

aggcggacaa agcccgattg ttcttgggcc ctttcccat cgcgctggg cctgctcccc 60  
 agcccggggc agggcgggg gccagtgtg tgacacacgc tgtagctgtc tccccggctg 120  
 gctggctcgc tctctcctgg ggacacagag gtcggcaggc agcacacaga gggacctacg 180  
 ggcagctgtt ccttcccccg actcaagaat ccccgagggc ccggaggcct gcagcaggag 240

181

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cggccatgaa gaagctgatg gtggtgctga gtctgattgc tgcagcctgg gcagaggagc 300
agaataagtt ggtgcatggc ggaccctgcg acaagacatc tcaccctac caagctgccc 360
tctacacctc gggccacttg ctctgtggtg gggtccttat ccatccactg tgggtcctca 420
cagctgcccc ctgcaaaaaa ccgaatcttc aggtcttcct ggggaagcat aaccttcggc 480
aaaggagag ttcccaggag cagagttctg ttgtccgggc tgtgatccac cctgactatg 540
atgccgctca ccatgaccag gacatcatgc tgttgccctt ggcacgcccc gccaaactct 600
ctgaactcat ccagccccctt cccctggaga gggactgctc agccaacacc accagctgcc 660
acatcctggg ctggggcaag acagcagatg gtgatttccc tgacaccatc cagtgtgcat 720
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aagatgaaga taaggatgat acagtctcca tcaggcagtg gctgttgaa agatttaaga 1440
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tatttt 1506

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&lt;210&gt; 169

&lt;211&gt; 244

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 169

```

Met Lys Lys Leu Met Val Val Leu Ser Leu Ile Ala Ala Ala Trp Ala
  1             5             10             15
Glu Glu Gln Asn Lys Leu Val His Gly Gly Pro Cys Asp Lys Thr Ser
          20             25             30
His Pro Tyr Gln Ala Ala Leu Tyr Thr Ser Gly His Leu Leu Cys Gly
          35             40             45
Gly Val Leu Ile His Pro Leu Trp Val Leu Thr Ala Ala His Cys Lys
          50             55             60
Lys Pro Asn Leu Gln Val Phe Leu Gly Lys His Asn Leu Arg Gln Arg
          65             70             75             80
Glu Ser Ser Gln Glu Ser Ser Val Val Arg Ala Val Ile His Pro
          85             90             95
Asp Tyr Asp Ala Ala Ser His Asp Gln Asp Ile Met Leu Leu Arg Leu
          100            105            110
Ala Arg Pro Ala Lys Leu Ser Glu Leu Ile Gln Pro Leu Pro Leu Glu
          115            120            125
Arg Asp Cys Ser Ala Asn Thr Thr Ser Cys His Ile Leu Gly Trp Gly
          130            135            140
Lys Thr Ala Asp Gly Asp Phe Pro Asp Thr Ile Gln Cys Ala Tyr Ile
          145            150            155            160
His Leu Val Ser Arg Glu Glu Cys Glu His Ala Tyr Pro Gly Gln Ile
          165            170            175
Thr Gln Asn Met Leu Cys Ala Gly Asp Glu Lys Tyr Gly Lys Asp Ser
          180            185            190
Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Gly Asp His Leu Arg
          195            200            205
Gly Leu Val Ser Trp Gly Asn Ile Pro Cys Gly Ser Lys Glu Lys Pro
          210            215            220
Gly Val Tyr Thr Asn Val Cys Arg Tyr Thr Asn Trp Ile Gln Lys Thr

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182

225  
Ile Gln Ala Lys

230

235

240

<210> 170  
<211> 1641  
<212> DNA  
<213> Homo sapiens

<400> 170  
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atccacttca gctccccggt attcacctcg cgctcagccg ccttctcggg ccgcggcgcc 120  
caggtgcgcc tgagctccgc tcgccccggc ggcttggca gcagcagcct ctacggcctc 180  
ggcgccctcg ggccgcgcgt ggccgtgcgc tctgcctatg ggggcccggg gggcgccggc 240  
atccgcgagg tcaccattaa ccagagccctg ctggccccgc tgcggctgga cgccgacccc 300  
tccctccagc ggggtgcgcca ggaggagagc gaggcagatca agaccctcaa caacaagttt 360  
gcctccttca tcgacaaggt gcggtttctg gaggcagcaga acaagctgct ggagaccaag 420  
tggacgctgc tgcaggagca gaagtcggcc aagagcagcc gcctcccaga catctttgag 480  
ggccagattg ctggccttcg gggtcagctt gaggcactgc aggtggatgg gggccgcctg 540  
gaggcgagc tgccggagcat gcaggatgtg gtggaggact tcaagaataa gtacgaagat 600  
gaaattaacc gccgcacagc tgctgagaat gattttgtgg tgctgaagaa ggatgtggat 660  
gctgcctaca cgagcaaggt ggagctggag gccaaagtg atgccctgaa tgatgagatc 720  
aacttcctca ggaccctcaa tgagacggag ttgacagagc tgcagtccca gatctccgac 780  
acatctgtgg tgctgtccat ggacaacagt cgctccctgg acctggacgg catcatcgct 840  
gaggtcaagg cacagtatga ggagatggcc aaatgcagcc gggctgaggc tgaagcctgg 900  
taccagacca agtttgagac cctccaggcc caggctggga agcatgggga cgacctcgg 960  
aatacccgga atgagatttc agagatgaac cgggccatcc agaggctgca ggctgagatc 1020  
gacaacatca agaaccagcg tgccaagtgt gaggccgcca ttgccgaggc tgaggagcgt 1080  
ggggagctgg cgctcaagga tgctcgtgcc aagcaggagg agctggaagc cgccctgcag 1140  
cgggccaagc aggatatggc acggcagctg cgtgagtacc aggaactcat gacgtgaa 1200  
ctggccctgg acatcgagat cgccacctac cgcaagctgc tggagggcga ggagagccgg 1260  
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agcagtggcg gtggcattgg gctgaccctc gggggaacca tgggcagcaa tgccctgagc 1380  
ttctccagca gtgcgggtcc tgggtcctg aaggcttatt ccatccggac cgcacccgcc 1440  
agtcgcagga gtgcccgcga ctgagccgcc tcccaccact ccaactcctc agccaccacc 1500  
cacaatcaca agaagattcc caccctgcc tccatgcct ggtcccaaga cagtgagaca 1560  
gtctggaaag tgatgtcaga atagcttcca ataaagcagc ctcatctga ggcctgagtg 1620  
atccaaaaaa aaaaaaaaaa a 1641

<210> 171  
<211> 469  
<212> PRT  
<213> Homo sapiens

<400> 171  
Met Ser Ile His Phe Ser Ser Pro Val Phe Thr Ser Arg Ser Ala Ala  
1 5 10 15  
Phe Ser Gly Arg Gly Ala Gln Val Arg Leu Ser Ser Ala Arg Pro Gly  
20 25 30  
Gly Leu Gly Ser Ser Ser Leu Tyr Gly Leu Gly Ala Ser Arg Pro Arg  
35 40 45  
Val Ala Val Arg Ser Ala Tyr Gly Gly Pro Val Gly Ala Gly Ile Arg  
50 55 60  
Glu Val Thr Ile Asn Gln Ser Leu Leu Ala Pro Leu Arg Leu Asp Ala  
65 70 75 80  
Asp Pro Ser Leu Gln Arg Val Arg Gln Glu Glu Ser Glu Gln Ile Lys  
85 90 95

183

Ala Leu Asn Asn Lys Phe Ala Ser Phe Ile Asp Lys Val Arg Phe Leu  
                   100                  105                  110  
 Glu Gln Gln Asn Lys Leu Leu Glu Thr Lys Trp Thr Leu Leu Gln Glu  
                   115                  120                  125  
 Gln Lys Ser Ala Lys Ser Ser Arg Leu Pro Asp Ile Phe Glu Ala Gln  
                   130                  135                  140  
 Ile Ala Gly Leu Arg Gly Gln Leu Glu Ala Leu Gln Val Asp Gly Gly  
 145                  150                  155                  160  
 Arg Leu Glu Gln Gly Leu Arg Thr Met Gln Asp Val Val Glu Asp Phe  
                   165                  170                  175  
 Lys Asn Lys Tyr Glu Asp Glu Ile Asn Arg Arg Thr Ala Ala Glu Asn  
                   180                  185                  190  
 Glu Phe Val Val Leu Lys Lys Asp Val Asp Ala Ala Tyr Met Ser Lys  
                   195                  200                  205  
 Val Glu Leu Glu Ala Lys Val Asp Ala Leu Asn Asp Glu Ile Asn Phe  
                   210                  215                  220  
 Leu Arg Thr Leu Asn Glu Thr Glu Leu Thr Glu Leu Gln Ser Gln Ile  
 225                  230                  235                  240  
 Ser Asp Thr Ser Val Leu Ser Met Asp Asn Ser Arg Ser Leu Asp  
                   245                  250                  255  
 Leu Asp Gly Ile Ile Ala Glu Val Lys Ala Gln Tyr Glu Glu Met Ala  
                   260                  265                  270  
 Lys Cys Ser Arg Ala Glu Ala Glu Ala Trp Tyr Gln Thr Lys Phe Glu  
                   275                  280                  285  
 Thr Leu Gln Ala Gln Ala Gly Lys His Gly Asp Asp Leu Arg Asn Thr  
                   290                  295                  300  
 Arg Asn Glu Ile Ser Glu Met Asn Arg Ala Ile Gln Arg Leu Gln Ala  
 305                  310                  315                  320  
 Glu Ile Asp Asn Ile Lys Asn Gln Arg Ala Lys Leu Glu Ala Ala Ile  
                   325                  330                  335  
 Ala Glu Ala Glu Glu Cys Gly Glu Leu Ala Leu Lys Asp Ala Arg Ala  
                   340                  345                  350  
 Lys Gln Glu Glu Leu Glu Ala Ala Leu Gln Arg Ala Lys Gln Asp Met  
                   355                  360                  365  
 Ala Arg Gln Leu Arg Glu Tyr Gln Glu Leu Met Ser Val Lys Leu Ala  
                   370                  375                  380  
 Leu Asp Ile Glu Ile Ala Thr Tyr Arg Lys Leu Leu Glu Gly Glu Glu  
 385                  390                  395                  400  
 Ser Arg Leu Ala Gly Asp Gly Val Gly Ala Val Asn Ile Ser Val Met  
                   405                  410                  415  
 Asn Ser Thr Gly Gly Ser Ser Ser Gly Gly Gly Ile Gly Leu Thr Leu  
                   420                  425                  430  
 Gly Gly Thr Met Gly Ser Asn Ala Leu Ser Phe Ser Ser Ser Ala Gly  
                   435                  440                  445  
 Pro Gly Leu Leu Lys Ala Tyr Ser Ile Arg Thr Ala Ser Ala Ser Arg  
                   450                  455                  460  
 Arg Ser Ala Arg Asp  
 465

&lt;210&gt; 172

&lt;211&gt; 1640

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 172

gcgagtgcgc gctcctcctc gcccgccgct aggtccatcc cggcccagcc accatgtcca 60  
 tccacttcag ctccccgcta ttacctcgc gctcagccgc cttctcgggc cgcggcgccc 120

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aggtgcgct gagctccgct cgccccggcg gccttggcag cagcagcctc tacggcctcg 180
gcgcctcgcg gccgcgcgtg gccgtgctg ctgcctatgg gggcccgtg ggccgcca 240
tccgcgaggt caccattaac cagagcctgc tggccccgtg gcggctggac gccgacct 300
ccctccagcg ggtgcgccag gaggagagcg agcagatcaa gacctcaac aacaagttg 360
cctccttcat cgacaagggt cggtttctgg agcagcagaa caagctgctg gagaccaagt 420
ggacgtgct gcaggagcag aagtcggcca agagcagccg cctcccagac atctttgagg 480
cccagattgc tggccttcgg ggtcagctg aggcactgca ggtggatggg ggccgctgg 540
aggcggagct gcggagcatg caggatgtgg tggaggactt caagaataag tacgaagatg 600
aaattaaccg ccgcacagct gctgagaatg agtttgtgg gctgaagaag gatgtggatg 660
ctgcctacat gagcaagggt gagctggagg ccaagggtga tgccctgaat gatgagatca 720
acttctcag gacctcaat gagacggagt tgacagagct gcagtcccag atctccgaca 780
catctgtggt gctgtccatg gacaacagtc gtcctctgga cctggacggc atcatcgctg 840
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accagaccaa gtttgagacc ctccaggccc aggctgggaa gcatggggac gacctccgga 960
atacccgaa tgagatttca gagatgaacc gggccatcca gaggctgcag gctgagatcg 1020
acaacatcaa gaaccagct gccaaagtgg aggcggccat tgccgaggct gaggagcgtg 1080
gggagctggc gctcaaggat gctcgtgcca agcaggagga gctggaagcc gccctgcagc 1140
gggccaagca ggatatggca cggcagctgc gtgagtacca ggaactcatg agcgtgaagc 1200
tggccttga catcgagatc gccacctacc gcaagctgct ggagggcgag gagagccggt 1260
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acaatcacia gaagattccc acccctgcct cccatgcctg gtcccaagac agtgagacag 1560
tctgaaaagt gatgtcagaa tagcttccaa taaagcagcc tcattctgag gcctgagtga 1620
tccaaaaaaa aaaaaaaaaa 1640

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&lt;210&gt; 173

&lt;211&gt; 469

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 173

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Met Ser Ile His Phe Ser Ser Pro Val Phe Thr Ser Arg Ser Ala Ala
 1           5           10           15
Phe Ser Gly Arg Gly Ala Gln Val Arg Leu Ser Ser Ala Arg Pro Gly
 20           25           30
Gly Leu Gly Ser Ser Ser Leu Tyr Gly Leu Gly Ala Ser Arg Pro Arg
 35           40           45
Val Ala Val Arg Ser Ala Tyr Gly Gly Pro Val Gly Ala Gly Ile Arg
 50           55           60
Glu Val Thr Ile Asn Gln Ser Leu Leu Ala Pro Leu Arg Leu Asp Ala
 65           70           75           80
Asp Pro Ser Leu Gln Arg Val Arg Gln Glu Glu Ser Glu Gln Ile Lys
 85           90           95
Thr Leu Asn Asn Lys Phe Ala Ser Phe Ile Asp Lys Val Arg Phe Leu
100          105          110
Glu Gln Gln Asn Lys Leu Leu Glu Thr Lys Trp Thr Leu Leu Gln Glu
115          120          125
Gln Lys Ser Ala Lys Ser Ser Arg Leu Pro Asp Ile Phe Glu Ala Gln
130          135          140
Ile Ala Gly Leu Arg Gly Gln Leu Glu Ala Leu Gln Val Asp Gly Gly
145          150          155          160
Arg Leu Glu Ala Glu Leu Arg Ser Met Gln Asp Val Val Glu Asp Phe
165          170          175
Lys Asn Lys Tyr Glu Asp Glu Ile Asn Arg Arg Thr Ala Ala Glu Asn
180          185          190
Glu Phe Val Val Leu Lys Lys Asp Val Asp Ala Ala Tyr Met Ser Lys

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185

195	200	205
Val Glu Leu Glu Ala Lys	Val Asp Ala Leu Asn	Asp Glu Ile Asn Phe
210	215	220
Leu Arg Thr Leu Asn Glu	Thr Glu Leu Thr Glu	Leu Gln Ser Gln Ile
225	230	235
Ser Asp Thr Ser Val Val	Leu Ser Met Asp Asn	Ser Arg Ser Leu Asp
245	250	255
Leu Asp Gly Ile Ile Ala	Glu Val Lys Ala Gln	Tyr Glu Glu Met Ala
260	265	270
Lys Cys Ser Arg Ala Glu	Ala Glu Ala Trp Tyr	Gln Thr Lys Phe Glu
275	280	285
Thr Leu Gln Ala Gln Ala	Gly Lys His Gly Asp	Asp Leu Arg Asn Thr
290	295	300
Arg Asn Glu Ile Ser Glu	Met Asn Arg Ala Ile	Gln Arg Leu Gln Ala
305	310	315
Glu Ile Asp Asn Ile Lys	Asn Gln Arg Ala Lys	Leu Glu Ala Ala Ile
325	330	335
Ala Glu Ala Glu Glu Arg	Gly Glu Leu Ala Leu	Lys Asp Ala Arg Ala
340	345	350
Lys Gln Glu Glu Leu Glu	Ala Ala Leu Gln Arg	Ala Lys Gln Asp Met
355	360	365
Ala Arg Gln Leu Arg Glu	Tyr Gln Glu Leu Met	Ser Val Lys Leu Ala
370	375	380
Leu Asp Ile Glu Ile Ala	Thr Tyr Arg Lys Leu	Leu Glu Gly Glu Glu
385	390	395
Ser Arg Leu Ala Gly Asp	Gly Val Gly Ala Val	Asn Ile Ser Val Met
405	410	415
Asn Ser Thr Gly Gly Ser	Ser Ser Ser Gly Gly	Gly Ile Gly Leu Thr Leu
420	425	430
Gly Gly Thr Met Gly Ser	Asn Ala Leu Ser Phe	Ser Ser Ser Ala Gly
435	440	445
Pro Gly Leu Leu Lys Ala	Tyr Ser Ile Arg Thr	Ala Ser Ala Ser Arg
450	455	460
Arg Ser Ala Arg Asp		
465		

&lt;210&gt; 174

&lt;211&gt; 2186

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 174

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acacggacca aggagtctaa cacgtgcgcg agtcgggggc tcgcacgaaa gccgcccgtgg 60
cgcaatgaag gtgaaggccg gcgcgctcgc cggccgaggt gggatcccga ggcctctcca 120
gtccgcccag ggcgaccac cgcccgtct cgcccgcgc gccggggagg tggagcacga 180
gcgcacgtgt taggaccgga aagatggtga actatgcctg ggcaggcgga agccagagga 240
aactctggtg gaggtccgta gcggtcctga cgtgcaaadc ggtcgtccga cctgggtata 300
ggggcgggct ccaggcgagg cggtcgacgc tctgaaaac ttgcgcgcgc gctcgcgcca 360
ctgcgcccgg agcgatgaag atggtcgcgc cctggacgcg gttctactcc aacagctgct 420
gcttggtgctg ccatgtccgc accggcacca tctgtctcgg cgtctggtat ctgatcatca 480
atgctgtggt actgttgatt ttattgagtg ccctggctga tccggatcag tataactttt 540
caagttctga actgggagg gactttgagt tcatggatga tgccaacatg tgcatgtcca 600
ttgcgatttc tcttctcatg atcctgatat gtgctatggc tacttacgga gcgtacaagc 660
aacgcgcagc ctgatcatc ccattcttct gttaccagat ctttgacttt gccctgaaca 720
tggttggttg aatcactgtg cttattttatc caaactccat tcaggaatac atacggcaac 780
tgccctctaa ttttccctac agagatgatg tcatgtcagt gaatcctacc tgtttggtcc 840
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186

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tttggaaactg ctaccgatac atcaatggta ggaactcctc tgatgtcctg gtttatgtta 960
ccagcaatga cactacgggtg ctgctacccc cgtatgatga tgccactgtg aatgggtgctg 1020
ccaaggagcc accgccacct tacgtgtctg cctaagcctt caagtgggcg gagctgaggg 1080
cagcagcttg actttgcaga catctgagca atagttctgt tatttcactt ttgccatgag 1140
cctctctgag cttgtttgtt gctgaaatgc tactttttaa aatttagatg ttagattgaa 1200
aactgtagtt ttcaacatat gctttgctag aacactgtga tagattaact gtagaattct 1260
tcctgtacga ttggggatat aatgggcttc actaaccttc cctaggcatt gaaacttccc 1320
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cttcagccat tccagcatag agaacaaaac cttatggaaa caggaatgtc aattgtgtaa 1500
tcattgttct aattaggtaa atagaagtcc ttatgtatgt gttacaagaa tttccccac 1560
aacatccttt atgactgaag ttcaatgaca gtttgtgttt ggggtgtaaa ggattttctc 1620
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actgttcttg tggatcttgt gtccaggac atgggggtgac atgcctcgta tgtgttagag 1740
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tccaaactgac tttatcaagt ggaattggga tatatttgat atacttctgc ctaacaacat 1920
ggaaaagggt tttcttttcc ctgcaagcta catcctactg ctttgaactt ccaagtatgt 1980
ctagtcacct tttaaaatgt aaacattttc agaaaaatga ggattgcctt ccttgatgc 2040
gctttttacc ttgactacct gaattgcaag ggatttttat atattcatat gttacaaagt 2100
cagcaactct cctgttggtt cattattgaa tgtgctgtaa attaagttgt ttgcaattaa 2160
aacaagggtt gccacaaaa aaaaaa 2186

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&lt;210&gt; 175

&lt;211&gt; 283

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 175

```

Met Val Asn Tyr Ala Trp Ala Gly Arg Ser Gln Arg Lys Leu Trp Trp
  1          5          10          15
Arg Ser Val Ala Val Leu Thr Cys Lys Ser Val Val Arg Pro Gly Tyr
      20          25          30
Arg Gly Gly Leu Gln Ala Arg Arg Ser Thr Leu Leu Lys Thr Cys Ala
      35          40          45
Arg Ala Arg Ala Thr Ala Pro Gly Ala Met Lys Met Val Ala Pro Trp
      50          55          60
Thr Arg Phe Tyr Ser Asn Ser Cys Cys Leu Cys Cys His Val Arg Thr
      65          70          75          80
Gly Thr Ile Leu Leu Gly Val Trp Tyr Leu Ile Ile Asn Ala Val Val
      85          90          95
Leu Leu Ile Leu Leu Ser Ala Leu Ala Asp Pro Asp Gln Tyr Asn Phe
      100          105          110
Ser Ser Ser Glu Leu Gly Gly Asp Phe Glu Phe Met Asp Asp Ala Asn
      115          120          125
Met Cys Ile Ala Ile Ala Ile Ser Leu Leu Met Ile Leu Ile Cys Ala
      130          135          140
Met Ala Thr Tyr Gly Ala Tyr Lys Gln Arg Ala Ala Trp Ile Ile Pro
      145          150          155          160
Phe Phe Cys Tyr Gln Ile Phe Asp Phe Ala Leu Asn Met Leu Val Ala
      165          170          175
Ile Thr Val Leu Ile Tyr Pro Asn Ser Ile Gln Glu Tyr Ile Arg Gln
      180          185          190
Leu Pro Pro Asn Phe Pro Tyr Arg Asp Asp Val Met Ser Val Asn Pro
      195          200          205
Thr Cys Leu Val Leu Ile Ile Leu Leu Phe Ile Ser Ile Ile Leu Thr
      210          215          220
Phe Lys Gly Tyr Leu Ile Ser Cys Val Trp Asn Cys Tyr Arg Tyr Ile

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187

225					230					235				240	
Asn	Gly	Arg	Asn	Ser	Ser	Asp	Val	Leu	Val	Tyr	Val	Thr	Ser	Asn	Asp
				245						250				255	
Thr	Thr	Val	Leu	Leu	Pro	Pro	Tyr	Asp	Asp	Ala	Thr	Val	Asn	Gly	Ala
			260					265					270		
Ala	Lys	Glu	Pro	Pro	Pro	Pro	Tyr	Val	Ser	Ala					
		275					280								

<210> 176  
 <211> 597  
 <212> DNA  
 <213> Homo sapiens

<400> 176  
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 caggactcca cctcagacct gatcccagcc ccacctctga gcaagggtccc tctgcagcag 120  
 aacttccagg acaaccaatt ccagggggaag tggatgttgg taggcctggc aggggaatgca 180  
 attctcagag aagacaaaaga cccgcaaaag atgtatgcca ccatctatga gctgaaagaa 240  
 gacaagagct acaatgtcac ctccgtcctg tttaggaaaa agaagtgtga ctactggatc 300  
 aggacttttg ttccagggtg ccagcccggc gagttcacgc tgggcaacat taagagttac 360  
 cctggattaa cgagttacct cgtccgagtg gtgagcacca actacaacca gcatgctatg 420  
 gtgttcttca agaaagtttc tcaaaacagg gagtacttca agatcacctt ctacggggaga 480  
 accaaggagc tgacttcgga actaaaggag aacttcatcc gcttctccaa atatctgggc 540  
 ctccctgaaa accacatcgt cttccctgtc ccaatcgacc agtgtatcga cggtctga 597

<210> 177  
 <211> 198  
 <212> PRT  
 <213> Homo sapiens

<400> 177  
 Met Pro Leu Gly Leu Leu Trp Leu Gly Leu Ala Leu Leu Gly Ala Leu  
 1 5 10 15  
 His Ala Gln Ala Gln Asp Ser Thr Ser Asp Leu Ile Pro Ala Pro Pro  
 20 25 30  
 Leu Ser Lys Val Pro Leu Gln Gln Asn Phe Gln Asp Asn Gln Phe Gln  
 35 40 45  
 Gly Lys Trp Tyr Val Val Gly Leu Ala Gly Asn Ala Ile Leu Arg Glu  
 50 55 60  
 Asp Lys Asp Pro Gln Lys Met Tyr Ala Thr Ile Tyr Glu Leu Lys Glu  
 65 70 75 80  
 Asp Lys Ser Tyr Asn Val Thr Ser Val Leu Phe Arg Lys Lys Lys Cys  
 85 90 95  
 Asp Tyr Trp Ile Arg Thr Phe Val Pro Gly Cys Gln Pro Gly Glu Phe  
 100 105 110  
 Thr Leu Gly Asn Ile Lys Ser Tyr Pro Gly Leu Thr Ser Tyr Leu Val  
 115 120 125  
 Arg Val Val Ser Thr Asn Tyr Asn Gln His Ala Met Val Phe Phe Lys  
 130 135 140  
 Lys Val Ser Gln Asn Arg Glu Tyr Phe Lys Ile Thr Leu Tyr Gly Arg  
 145 150 155 160  
 Thr Lys Glu Leu Thr Ser Glu Leu Lys Glu Asn Phe Ile Arg Phe Ser  
 165 170 175  
 Lys Tyr Leu Gly Leu Pro Glu Asn His Ile Val Phe Pro Val Pro Ile  
 180 185 190  
 Asp Gln Cys Ile Asp Gly  
 195

<210> 178  
 <211> 1518  
 <212> DNA  
 <213> Homo sapiens

<400> 178

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ccccggggcc gccctgaccg gggagcagct cctgggcagc ctgctgcggc agctgcagct 180
caaagaggtg cccaccctgg acagggccga catggaggag ctggtcatcc ccaccacgt 240
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caaccgcacc tccctcatcg actccaggct ggtgtccgtc cagcagagcg gctggaaggc 600
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```

<210> 179  
 <211> 366  
 <212> PRT  
 <213> Homo sapiens

<400> 179

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  1          5          10          15
Ser Pro Gly Ala Ala Leu Thr Gly Glu Gln Leu Leu Gly Ser Leu Leu
          20          25          30
Arg Gln Leu Gln Leu Lys Glu Val Pro Thr Leu Asp Arg Ala Asp Met
          35          40          45
Glu Glu Leu Val Ile Pro Thr His Val Arg Ala Gln Tyr Val Ala Leu
          50          55          60
Leu Gln Arg Ser His Gly Asp Arg Ser Arg Gly Lys Arg Phe Ser Gln
          65          70          75          80
Ser Phe Arg Glu Val Ala Gly Arg Phe Leu Ala Leu Glu Ala Ser Thr
          85          90          95
His Leu Leu Val Phe Gly Met Glu Gln Arg Leu Pro Pro Asn Ser Glu
          100          105          110
Leu Val Gln Ala Val Leu Arg Leu Phe Gln Glu Pro Val Pro Lys Ala
          115          120          125
Ala Leu His Arg His Gly Arg Leu Ser Pro Arg Ser Ala Arg Ala Arg
```

189

130	135	140
Val Thr Val Glu Trp Leu Arg Val Arg Asp Asp Gly Ser Asn Arg Thr		
145	150	155
Ser Leu Ile Asp Ser Arg Leu Val Ser Val His Glu Ser Gly Trp Lys		160
	165	170
Ala Phe Asp Val Thr Glu Ala Val Asn Phe Trp Gln Gln Leu Ser Arg		175
	180	185
Pro Arg Gln Pro Leu Leu Leu Gln Val Ser Val Gln Arg Glu His Leu		190
	195	200
Gly Pro Leu Ala Ser Gly Ala His Lys Leu Val Arg Phe Ala Ser Gln		205
	210	215
Gly Ala Pro Ala Gly Leu Gly Glu Pro Gln Leu Glu Leu His Thr Leu		220
225	230	235
Asp Leu Gly Asp Tyr Gly Ala Gln Gly Asp Cys Asp Pro Glu Ala Pro		240
	245	250
Met Thr Glu Gly Thr Arg Cys Cys Arg Gln Glu Met Tyr Ile Asp Leu		255
	260	265
Gln Gly Met Lys Trp Ala Glu Asn Trp Val Leu Glu Pro Pro Gly Phe		270
	275	280
Leu Ala Tyr Glu Cys Val Gly Thr Cys Arg Gln Pro Pro Glu Ala Leu		285
	290	295
Ala Phe Lys Trp Pro Phe Leu Gly Pro Arg Gln Cys Ile Ala Ser Glu		300
305	310	315
Thr Asp Ser Leu Pro Met Ile Val Ser Ile Lys Glu Gly Gly Arg Thr		320
	325	330
Arg Pro Gln Val Ser Leu Pro Asn Met Arg Val Gln Lys Cys Ser		335
	340	345
Cys Ala Ser Asp Gly Ala Leu Val Pro Arg Arg Leu Gln Pro		350
	355	360
		365

&lt;210&gt; 180

&lt;211&gt; 444

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 180

```

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accatgaagc tgtcgggtgtg tctcctgctg gtcacgctgg ccctctgctg ctaccaggcc 120
aatgccgagt tctgcccagc tcttggttct gagctgttag acttcttctt cattagttaa 180
cctctgttca agttaagtct tgccaaattt gatgccctc cggaagctgt tgcagccaag 240
ttaggagtga agagatgcac ggatcagatg tcccttcaga aacgaagcct cattgcggaa 300
gtcctggtga aaatattgaa gaaatgtagt gtgtgacatg taaaaacttt catcctgggt 360
tccactgtct ttcaatgaca ccctgatctt cactgcagaa tgtaaagggt tcaacgtctt 420
gctttaataa atcacttgct ctac                                     444

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&lt;210&gt; 181

&lt;211&gt; 90

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 181

Met Lys Leu Ser Val Cys Leu Leu Leu Val Thr Leu Ala Leu Cys Cys
1 5 10 15
Tyr Gln Ala Asn Ala Glu Phe Cys Pro Ala Leu Val Ser Glu Leu Leu
20 25 30
Asp Phe Phe Phe Ile Ser Glu Pro Leu Phe Lys Leu Ser Leu Ala Lys
35 40 45

190

Phe Asp Ala Pro Pro Glu Ala Val Ala Ala Lys Leu Gly Val Lys Arg  
 50 55 60  
 Cys Thr Asp Gln Met Ser Leu Gln Lys Arg Ser Leu Ile Ala Glu Val  
 65 70 75 80  
 Leu Val Lys Ile Leu Lys Lys Cys Ser Val  
 85 90

<210> 182  
 <211> 754  
 <212> DNA  
 <213> Homo sapiens

<400> 182  
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 aggaaagcat aggaggtttg aaatggaccg ggaacctaag agtgccagat actgtgctga 180  
 gtgtaatagg ctgcatcctg ctgaggaagg agacttttgg gcagagtcaa gcatgttggg 240  
 cctcaagatc acctactttg cactgatgga tggaaagggt tatgacatca cagagtgggc 300  
 tggatgccag cgtgtaggta tctcccaga taccacaga gtcccctatc acatctcatt 360  
 tggttctcgg attccaggca ccagaggcg gcagagagcc accccagatg cccctcctgc 420  
 tgatcttcag gatttcttga gtggatctt tcaagtaccc ccagggcaga tgccaatggg 480  
 aacttctttg cagctcctca gctgcccct ggagccgctg cagcctctaa gcccaacagc 540  
 acagtaccca agggagaagc caaacctaag cggcggaaga aagtgaggag gcccttccaa 600  
 cgttgatgcc ccttctcttt cctcaaatca atgtcaggga gtcaaaaggg ctgtagcaca 660  
 ggatggagtt tgatttatcc ctctccccc aacacctagg aactgaatct ttttcttttt 720  
 attttttgag atggagtctt gctctgttgc ccag 754

<210> 183  
 <211> 191  
 <212> PRT  
 <213> Homo sapiens

<400> 183  
 Met Lys Arg Met Ala Glu Asn Glu Leu Ser Arg Ser Val Asn Glu Phe  
 1 5 10 15  
 Leu Ser Lys Leu Gln Asp Asp Leu Lys Glu Ala Met Asn Thr Met Met  
 20 25 30  
 Cys Ser Arg Cys Gln Gly Lys His Arg Arg Phe Glu Met Asp Arg Glu  
 35 40 45  
 Pro Lys Ser Ala Arg Tyr Cys Ala Glu Cys Asn Arg Leu His Pro Ala  
 50 55 60  
 Glu Glu Gly Asp Phe Trp Ala Glu Ser Ser Met Leu Gly Leu Lys Ile  
 65 70 75 80  
 Thr Tyr Phe Ala Leu Met Asp Gly Lys Val Tyr Asp Ile Thr Glu Trp  
 85 90 95  
 Ala Gly Cys Gln Arg Val Gly Ile Ser Pro Asp Thr His Arg Val Pro  
 100 105 110  
 Tyr His Ile Ser Phe Gly Ser Arg Ile Pro Gly Thr Arg Gly Arg Gln  
 115 120 125  
 Arg Ala Thr Pro Asp Ala Pro Pro Ala Asp Leu Gln Asp Phe Leu Ser  
 130 135 140  
 Arg Ile Phe Gln Val Pro Pro Gly Gln Met Pro Met Gly Thr Ser Leu  
 145 150 155 160  
 Gln Leu Leu Ser Leu Pro Leu Glu Pro Leu Gln Pro Leu Ser Pro Thr  
 165 170 175  
 Ala Gln Tyr Pro Arg Glu Lys Pro Asn Leu Ser Gly Gly Arg Lys  
 180 185 190

191

<210> 184  
<211> 2511  
<212> DNA  
<213> Homo sapiens

<400> 184  
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tcccctccac gatgtatggg gacccgcatg cagccaggtc catgcagccg gtccaccacc 180  
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aagatatagc cgtgttcgcc aaacagattc gcgcagaaaa acctctattt tcttctaate 480  
cagaactgga taacttgatg attcaagcca tacaagtatt aagggttcat ctattggaat 540  
tagagaaggc acacgaatta tgtgacaatt tctgccaccg gtatattagc tgtttgaaag 600  
ggaaaatgcc tatcgatttg gtgatagacg atagagaagg aggatcaaaa tcagacagtg 660  
aagatataac aagatcagca aatctaactc accagccctc ttggaacaga gatcatgatg 720  
acacggcatc tactcgttca ggaggaaccc caggcccttc cagcgggtggc cacacgtcac 780  
acagtgggga caacagcagt gagcaagggt atggcttgga caacagtgtg gcttccccca 840  
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tttgtgcaaa aaggactgga aaaatgaact gtattattgc aatttttttt t 2511

<210> 185  
<211> 390  
<212> PRT  
<213> Homo sapiens

<400> 185  
Met Ala Gln Arg Tyr Asp Asp Leu Pro His Tyr Gly Gly Met Asp Gly

192

1	5	10	15
Val Gly Ile Pro Ser Thr Met Tyr Gly Asp Pro His Ala Ala Arg Ser			
20	25	30	
Met Gln Pro Val His His Leu Asn His Gly Pro Pro Leu His Ser His			
35	40	45	
Gln Tyr Pro His Thr Ala His Thr Asn Ala Met Ala Pro Ser Met Gly			
50	55	60	
Ser Ser Val Asn Asp Ala Leu Lys Arg Asp Lys Asp Ala Ile Tyr Gly			
65	70	75	80
His Pro Leu Phe Pro Leu Leu Ala Leu Ile Phe Glu Lys Cys Glu Leu			
85	90	95	
Ala Thr Cys Thr Pro Arg Glu Pro Gly Val Ala Gly Gly Asp Val Cys			
100	105	110	
Ser Ser Glu Ser Phe Asn Glu Asp Ile Ala Val Phe Ala Lys Gln Ile			
115	120	125	
Arg Ala Glu Lys Pro Leu Phe Ser Ser Asn Pro Glu Leu Asp Asn Leu			
130	135	140	
Met Ile Gln Ala Ile Gln Val Leu Arg Phe His Leu Leu Glu Leu Glu			
145	150	155	160
Lys Val His Glu Leu Cys Asp Asn Phe Cys His Arg Tyr Ile Ser Cys			
165	170	175	
Leu Lys Gly Lys Met Pro Ile Asp Leu Val Ile Asp Asp Arg Glu Gly			
180	185	190	
Gly Ser Lys Ser Asp Ser Glu Asp Ile Thr Arg Ser Ala Asn Leu Thr			
195	200	205	
Asp Gln Pro Ser Trp Asn Arg Asp His Asp Asp Thr Ala Ser Thr Arg			
210	215	220	
Ser Gly Gly Thr Pro Gly Pro Ser Ser Gly Gly His Thr Ser His Ser			
225	230	235	240
Gly Asp Asn Ser Ser Glu Gln Gly Asp Gly Leu Asp Asn Ser Val Ala			
245	250	255	
Ser Pro Ser Thr Gly Asp Asp Asp Asp Pro Asp Lys Asp Lys Lys Arg			
260	265	270	
His Lys Lys Arg Gly Ile Phe Pro Lys Val Ala Thr Asn Ile Met Arg			
275	280	285	
Ala Trp Leu Phe Gln His Leu Thr His Pro Tyr Pro Ser Glu Glu Gln			
290	295	300	
Lys Lys Gln Leu Ala Gln Asp Thr Gly Leu Thr Ile Leu Gln Val Asn			
305	310	315	320
Asn Trp Phe Ile Asn Ala Arg Arg Arg Ile Val Gln Pro Met Ile Asp			
325	330	335	
Gln Ser Asn Arg Ala Val Ser Gln Gly Thr Pro Tyr Asn Pro Asp Gly			
340	345	350	
Gln Pro Met Gly Gly Phe Val Met Asp Gly Gln Gln His Met Gly Ile			
355	360	365	
Arg Ala Pro Gly Pro Met Ser Gly Met Gly Met Asn Met Gly Met Glu			
370	375	380	
Gly Gln Trp His Tyr Met			
385	390		

&lt;210&gt; 186

&lt;211&gt; 517

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 186

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193

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 acctgaatac aaagagcttc ttcaagagtt catagacagt gatgccgctg cagaggctat 240  
 ggggaaattc aagcagtgtt tctcaacca gtcacataga actctgaaaa actttggact 300  
 gatgatgcat acagtgtacg acagcatttg gtgtaatatg aagagtaatt aactttaccc 360  
 aaggcgtttg gctcagaggg ctacagacta tggccagaac tcatctgttg attgctagaa 420  
 accacttttc tttcttgtgt tgtcttttta tgtggaaact gctagacaac tgttgaaacc 480  
 tcaaattcat ttccatttca ataactaact gcaaatc 517

&lt;210&gt; 187

&lt;211&gt; 95

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 187

Met	Lys	Leu	Leu	Met	Val	Leu	Met	Leu	Ala	Ala	Leu	Leu	Leu	His	Cys
1				5					10					15	
Tyr	Ala	Asp	Ser	Gly	Cys	Lys	Leu	Leu	Glu	Asp	Met	Val	Glu	Lys	Thr
			20					25					30		
Ile	Asn	Ser	Asp	Ile	Ser	Ile	Pro	Glu	Tyr	Lys	Glu	Leu	Leu	Gln	Glu
			35				40					45			
Phe	Ile	Asp	Ser	Asp	Ala	Ala	Ala	Glu	Ala	Met	Gly	Lys	Phe	Lys	Gln
	50					55					60				
Cys	Phe	Leu	Asn	Gln	Ser	His	Arg	Thr	Leu	Lys	Asn	Phe	Gly	Leu	Met
65					70					75				80	
Met	His	Thr	Val	Tyr	Asp	Ser	Ile	Trp	Cys	Asn	Met	Lys	Ser	Asn	
			85						90					95	

&lt;210&gt; 188

&lt;211&gt; 2048

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 188

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 aaaagtggcc ccggacgcgc gagcctgagg attctgcaca aaagaggtgc ccaaaatgaa 180  
 gaccctgatg cgccatggtc tggcagtgtg tttagcgctc accaccatgt gcaccagctt 240  
 gttgctagtg tacagcagcc tcggcggcca gaaggagcgg ccccgccagc agcagcagca 300  
 gcagcagcaa cagcagcagc aggcgtcggc caccggcagc tcgcagccgg cggcggagag 360  
 cagcaccag cagcgcgccg gggtecccg gggaccggc cactggacg gatacctcg 420  
 agtggcggac cacaagcccc tgaaaatgca ctgcaggac tgtgccctgg tgaccagctc 480  
 agggcatctg ctgcacagtc ggcaaggctc ccagattgac cagacagagt gtgtcatccg 540  
 catgaatgac gccccacac gcggctatgg gcgtgacgtg ggcaatcgca ccagcctgag 600  
 ggtcatcgcg cattccagca tccagaggat cctccgcaac cgccatgacc tgctcaacgt 660  
 gagccagggc accgtgttca tcttctgggg ccccgagcgc tacatgcggc gggacggcaa 720  
 gggccaggtc tacaacaacc tgcattcctt gagccagggt ctgccccggc tgaaggcctt 780  
 catgattact cgccacaaga tgctgcagtt tgatgagctc ttcaagcagg agactggcaa 840  
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 agactgtaat ccaggtatt cactgcatca gacaccgaga cactgaactt cctgagccac 1260  
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194

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aaactgctct tttgtaaaaa gaatagcgat gacattttct aatgtgcaga aatgttccaa 1980
aaggacaaaa ttgaaaacca aaaactatgt tattaataca aaaaaatgct aaaaaaaaaa 2040
aaaaaaaaa                                     2048

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&lt;210&gt; 189

&lt;211&gt; 336

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 189

```

Met Lys Thr Leu Met Arg His Gly Leu Ala Val Cys Leu Ala Leu Thr
 1           5           10           15
Thr Met Cys Thr Ser Leu Leu Leu Val Tyr Ser Ser Leu Gly Gly Gln
 20           25           30
Lys Glu Arg Pro Pro Gln Gln Gln Gln Gln Gln Gln Gln Gln
 35           40           45
Gln Ala Ser Ala Thr Gly Ser Ser Gln Pro Ala Ala Glu Ser Ser Thr
 50           55           60
Gln Gln Arg Pro Gly Val Pro Ala Gly Pro Arg Pro Leu Asp Gly Tyr
 65           70           75           80
Leu Gly Val Ala Asp His Lys Pro Leu Lys Met His Cys Arg Asp Cys
 85           90           95
Ala Leu Val Thr Ser Ser Gly His Leu Leu His Ser Arg Gln Gly Ser
 100          105          110
Gln Ile Asp Gln Thr Glu Cys Val Ile Arg Met Asn Asp Ala Pro Thr
 115          120          125
Arg Gly Tyr Gly Arg Asp Val Gly Asn Arg Thr Ser Leu Arg Val Ile
 130          135          140
Ala His Ser Ser Ile Gln Arg Ile Leu Arg Asn Arg His Asp Leu Leu
 145          150          155          160
Asn Val Ser Gln Gly Thr Val Phe Ile Phe Trp Gly Pro Ser Ser Tyr
 165          170          175
Met Arg Arg Asp Gly Lys Gly Gln Val Tyr Asn Asn Leu His Leu Leu
 180          185          190
Ser Gln Val Leu Pro Arg Leu Lys Ala Phe Met Ile Thr Arg His Lys
 195          200          205
Met Leu Gln Phe Asp Glu Leu Phe Lys Gln Glu Thr Gly Lys Asp Arg
 210          215          220
Lys Ile Ser Asn Thr Trp Leu Ser Thr Gly Trp Phe Thr Met Thr Ile
 225          230          235          240
Ala Leu Glu Leu Cys Asp Arg Ile Asn Val Tyr Gly Met Val Pro Pro
 245          250          255
Asp Phe Cys Arg Asp Pro Asn His Pro Ser Val Pro Tyr His Tyr Tyr
 260          265          270
Glu Pro Phe Gly Pro Asp Glu Cys Thr Met Tyr Leu Ser His Glu Arg
 275          280          285
Gly Arg Lys Gly Ser His His Arg Phe Ile Thr Glu Lys Arg Val Phe
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Lys Asn Trp Ala Arg Thr Phe Asn Ile His Phe Phe Gln Pro Asp Trp

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			20					25					30			
Glu	Gln	Ala	Gln	Asp	Tyr	Leu	Lys	Arg	Phe	Tyr	Leu	Tyr	Asp	Ser	Glu	
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Thr	Lys	Asn	Ala	Asn	Ser	Leu	Glu	Ala	Lys	Leu	Lys	Glu	Met	Gln	Lys	
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Phe	Phe	Gly	Leu	Pro	Ile	Thr	Gly	Met	Leu	Asn	Ser	Arg	Val	Ile	Glu	
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Ile	Met	Gln	Lys	Pro	Arg	Cys	Gly	Val	Pro	Asp	Val	Ala	Glu	Tyr	Ser	
				85					90					95		
Leu	Phe	Pro	Asn	Ser	Pro	Lys	Trp	Thr	Ser	Lys	Val	Val	Thr	Tyr	Arg	
			100					105					110			
Ile	Val	Ser	Tyr	Thr	Arg	Asp	Leu	Pro	His	Ile	Thr	Val	Asp	Arg	Leu	
		115					120					125				
Val	Ser	Lys	Ala	Leu	Asn	Met	Trp	Gly	Lys	Glu	Ile	Pro	Leu	His	Phe	
		130				135					140					
Arg	Lys	Val	Val	Trp	Gly	Thr	Ala	Asp	Ile	Met	Ile	Gly	Phe	Ala	Arg	
145					150					155					160	
Gly	Ala	His	Gly	Asp	Ser	Tyr	Pro	Phe	Asp	Gly	Pro	Gly	Asn	Thr	Leu	
				165					170					175		

196

Ala His Ala Phe Ala Pro Gly Thr Gly Leu Gly Gly Asp Ala His Phe  
 180 185 190  
 Asp Glu Asp Glu Arg Trp Thr Asp Gly Ser Ser Leu Gly Ile Asn Phe  
 195 200 205  
 Leu Tyr Ala Ala Thr His Glu Leu Gly His Ser Leu Gly Met Gly His  
 210 215 220  
 Ser Ser Asp Pro Asn Ala Val Met Tyr Pro Thr Tyr Gly Asn Gly Asp  
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 Pro Gln Asn Phe Lys Leu Ser Gln Asp Asp Ile Lys Gly Ile Gln Lys  
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 Leu Tyr Gly Lys Arg Ser Asn Ser Arg Lys Lys  
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 <211> 2217  
 <212> DNA  
 <213> Homo sapiens

<400> 192  
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197

<210> 193  
 <211> 702  
 <212> PRT  
 <213> Homo sapiens

<400> 193

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Ala	Leu	Gly	Ser	Leu	Leu	Phe	Leu	Leu	Phe	Ser	Leu	Gly	Trp	Val	Gln
		20					25					30			
Pro	Ser	Arg	Thr	Leu	Ala	Gly	Glu	Thr	Gly	Gln	Glu	Ala	Ala	Pro	Leu
	35					40					45				
Asp	Gly	Val	Leu	Ala	Asn	Pro	Pro	Asn	Ile	Ser	Ser	Leu	Ser	Pro	Arg
50					55					60					
Gln	Leu	Leu	Gly	Phe	Pro	Cys	Ala	Glu	Val	Ser	Gly	Leu	Ser	Thr	Glu
65				70						75					80
Arg	Val	Arg	Glu	Leu	Ala	Val	Ala	Leu	Ala	Gln	Lys	Asn	Val	Lys	Leu
			85					90						95	
Ser	Thr	Glu	Gln	Leu	Arg	Cys	Leu	Ala	His	Arg	Leu	Ser	Glu	Pro	Pro
		100						105					110		
Glu	Asp	Leu	Asp	Ala	Leu	Pro	Leu	Asp	Leu	Leu	Leu	Phe	Leu	Asn	Pro
	115						120					125			
Asp	Ala	Phe	Ser	Gly	Pro	Gln	Ala	Cys	Thr	Arg	Phe	Phe	Ser	Arg	Ile
130						135				140					
Thr	Lys	Ala	Asn	Val	Asp	Leu	Leu	Pro	Arg	Gly	Ala	Pro	Glu	Arg	Gln
145				150						155					160
Arg	Leu	Leu	Pro	Ala	Ala	Leu	Ala	Cys	Trp	Gly	Val	Arg	Gly	Ser	Leu
			165					170						175	
Leu	Ser	Glu	Ala	Asp	Val	Arg	Ala	Leu	Gly	Gly	Leu	Ala	Cys	Asp	Leu
		180						185					190		
Pro	Gly	Arg	Phe	Val	Ala	Glu	Ser	Ala	Glu	Val	Leu	Leu	Pro	Arg	Leu
	195						200					205			
Val	Ser	Cys	Pro	Gly	Pro	Leu	Asp	Gln	Asp	Gln	Gln	Glu	Ala	Ala	Arg
210						215					220				
Ala	Ala	Leu	Gln	Gly	Gly	Gly	Pro	Pro	Tyr	Gly	Pro	Pro	Ser	Thr	Trp
225				230						235					240
Ser	Val	Ser	Thr	Met	Asp	Ala	Leu	Arg	Gly	Leu	Leu	Pro	Val	Leu	Gly
			245					250					255		
Gln	Pro	Ile	Ile	Arg	Ser	Ile	Pro	Gln	Gly	Ile	Val	Ala	Ala	Trp	Arg
		260						265					270		
Gln	Arg	Ser	Ser	Arg	Asp	Pro	Ser	Trp	Arg	Gln	Pro	Glu	Arg	Thr	Ile
	275						280					285			
Leu	Arg	Pro	Arg	Phe	Arg	Arg	Glu	Val	Glu	Lys	Thr	Ala	Cys	Pro	Ser
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Gly	Lys	Lys	Ala	Arg	Glu	Ile	Asp	Glu	Ser	Leu	Ile	Phe	Tyr	Lys	Lys
305				310						315					320
Trp	Glu	Leu	Glu	Ala	Cys	Val	Asp	Ala	Ala	Leu	Leu	Ala	Thr	Gln	Met
			325					330						335	
Asp	Arg	Val	Asn	Ala	Ile	Pro	Phe	Thr	Tyr	Glu	Gln	Leu	Asp	Val	Leu
		340						345					350		
Lys	His	Lys	Leu	Asp	Glu	Leu	Tyr	Pro	Gln	Gly	Tyr	Pro	Glu	Ser	Val
	355						360						365		
Ile	Gln	His	Leu	Gly	Tyr	Leu	Phe	Leu	Lys	Met	Ser	Pro	Glu	Asp	Ile
370					375						380				
Arg	Lys	Trp	Asn	Val	Thr	Ser	Leu	Glu	Thr	Leu	Lys	Ala	Leu	Leu	Glu
385				390						395					400
Val	Asn	Lys	Gly	His	Glu	Met	Ser	Pro	Gln	Ala	Pro	Arg	Arg	Pro	Leu
			405						410					415	

198

Pro Gln Val Ala Thr Leu Ile Asp Arg Phe Val Lys Gly Arg Gly Gln  
                   420                  425                  430  
 Leu Asp Lys Asp Thr Leu Asp Thr Leu Thr Ala Phe Tyr Pro Gly Tyr  
           435                  440                  445  
 Leu Cys Ser Leu Ser Pro Glu Leu Ser Ser Val Pro Pro Ser Ser  
           450                  455                  460  
 Ile Trp Ala Val Arg Pro Gln Asp Leu Asp Thr Cys Asp Pro Arg Gln  
           465                  470                  475                  480  
 Leu Asp Val Leu Tyr Pro Lys Ala Arg Leu Ala Phe Gln Asn Met Asn  
                   485                  490                  495  
 Gly Ser Glu Tyr Phe Val Lys Ile Gln Ser Phe Leu Gly Gly Ala Pro  
                   500                  505                  510  
 Thr Glu Asp Leu Lys Ala Leu Ser Gln Gln Asn Val Ser Met Asp Leu  
                   515                  520                  525  
 Ala Thr Phe Met Lys Leu Arg Thr Asp Ala Val Leu Pro Leu Thr Val  
                   530                  535                  540  
 Ala Glu Val Gln Lys Leu Leu Gly Pro His Val Glu Gly Leu Lys Ala  
                   545                  550                  555                  560  
 Glu Glu Arg His Arg Pro Val Arg Asp Trp Ile Leu Arg Gln Arg Gln  
                   565                  570                  575  
 Asp Asp Leu Asp Thr Leu Gly Leu Gly Leu Gln Gly Gly Ile Pro Asn  
                   580                  585                  590  
 Gly Tyr Leu Val Leu Asp Leu Ser Val Gln Gly Gly Arg Gly Gly Gln  
                   595                  600                  605  
 Ala Arg Ala Gly Gly Arg Ala Gly Gly Val Glu Val Gly Ala Leu Ser  
                   610                  615                  620  
 His Pro Ser Leu Cys Arg Gly Pro Leu Gly Asp Ala Leu Pro Pro Arg  
                   625                  630                  635                  640  
 Thr Trp Thr Cys Ser His Arg Pro Gly Thr Ala Pro Ser Leu His Pro  
                   645                  650                  655  
 Gly Leu Arg Ala Pro Leu Pro Cys Trp Pro Gln Pro Cys Trp Gly Ser  
                   660                  665                  670  
 Pro Pro Gly Gln Glu Gln Ala Arg Val Ile Pro Val Pro Pro Gln Glu  
                   675                  680                  685  
 Asn Ser Arg Ser Val Asn Gly Asn Met Pro Pro Ala Asp Thr  
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&lt;210&gt; 194

&lt;211&gt; 2135

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 194

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199

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&lt;210&gt; 195

&lt;211&gt; 630

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 195

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      20                      25                      30
Pro Ser Arg Thr Leu Ala Gly Glu Thr Gly Gln Glu Ala Ala Pro Leu
      35                      40                      45
Asp Gly Val Leu Ala Asn Pro Pro Asn Ile Ser Ser Leu Ser Pro Arg
      50                      55                      60
Gln Leu Leu Gly Phe Pro Cys Ala Glu Val Ser Gly Leu Ser Thr Glu
      65                      70                      75                      80
Arg Val Arg Glu Leu Ala Val Ala Leu Ala Gln Lys Asn Val Lys Leu
      85                      90                      95
Ser Thr Glu Gln Leu Arg Cys Leu Ala His Arg Leu Ser Glu Pro Pro
      100                     105                     110
Glu Asp Leu Asp Ala Leu Pro Leu Asp Leu Leu Leu Phe Leu Asn Pro
      115                     120                     125
Asp Ala Phe Ser Gly Pro Gln Ala Cys Thr Arg Phe Phe Ser Arg Ile
      130                     135                     140
Thr Lys Ala Asn Val Asp Leu Leu Pro Arg Gly Ala Pro Glu Arg Gln
      145                     150                     155                     160
Arg Leu Leu Pro Ala Ala Leu Ala Cys Trp Gly Val Arg Gly Ser Leu
      165                     170                     175
Leu Ser Glu Ala Asp Val Arg Ala Leu Gly Gly Leu Ala Cys Asp Leu
      180                     185                     190
Pro Gly Arg Phe Val Ala Glu Ser Ala Glu Val Leu Leu Pro Arg Leu
      195                     200                     205
Val Ser Cys Pro Gly Pro Leu Asp Gln Asp Gln Gln Glu Ala Ala Arg
      210                     215                     220
Ala Ala Leu Gln Gly Gly Gly Pro Pro Tyr Gly Pro Pro Ser Thr Trp

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200

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Gln	Pro	Ile	Ile	Arg	Ser	Ile	Pro	Gln	Gly	Ile	Val	Ala	Ala	Trp	Arg
				260					265					270	
Gln	Arg	Ser	Ser	Arg	Asp	Pro	Ser	Trp	Arg	Gln	Pro	Glu	Arg	Thr	Ile
		275					280					285			
Leu	Arg	Pro	Arg	Phe	Arg	Arg	Glu	Val	Glu	Lys	Thr	Ala	Cys	Pro	Ser
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Gly	Lys	Lys	Ala	Arg	Glu	Ile	Asp	Glu	Ser	Leu	Ile	Phe	Tyr	Lys	Lys
305					310					315					320
Trp	Glu	Leu	Glu	Ala	Cys	Val	Asp	Ala	Ala	Leu	Leu	Ala	Thr	Gln	Met
				325					330						335
Asp	Arg	Val	Asn	Ala	Ile	Pro	Phe	Thr	Tyr	Glu	Gln	Leu	Asp	Val	Leu
			340					345					350		
Lys	His	Lys	Leu	Asp	Glu	Leu	Tyr	Pro	Gln	Gly	Tyr	Pro	Glu	Ser	Val
		355					360						365		
Ile	Gln	His	Leu	Gly	Tyr	Leu	Phe	Leu	Lys	Met	Ser	Pro	Glu	Asp	Ile
		370				375					380				
Arg	Lys	Trp	Asn	Val	Thr	Ser	Leu	Glu	Thr	Leu	Lys	Ala	Leu	Leu	Glu
385					390					395					400
Val	Asn	Lys	Gly	His	Glu	Met	Ser	Pro	Gln	Ala	Pro	Arg	Arg	Pro	Leu
				405					410					415	
Pro	Gln	Val	Ala	Thr	Leu	Ile	Asp	Arg	Phe	Val	Lys	Gly	Arg	Gly	Gln
			420					425					430		
Leu	Asp	Lys	Asp	Thr	Leu	Asp	Thr	Leu	Thr	Ala	Phe	Tyr	Pro	Gly	Tyr
		435					440					445			
Leu	Cys	Ser	Leu	Ser	Pro	Glu	Glu	Leu	Ser	Ser	Val	Pro	Pro	Ser	Ser
		450				455					460				
Ile	Trp	Ala	Val	Arg	Pro	Gln	Asp	Leu	Asp	Thr	Cys	Asp	Pro	Arg	Gln
465					470					475					480
Leu	Asp	Val	Leu	Tyr	Pro	Lys	Ala	Arg	Leu	Ala	Phe	Gln	Asn	Met	Asn.
				485					490					495	
Gly	Ser	Glu	Tyr	Phe	Val	Lys	Ile	Gln	Ser	Phe	Leu	Gly	Gly	Ala	Pro
			500					505					510		
Thr	Glu	Asp	Leu	Lys	Ala	Leu	Ser	Gln	Gln	Asn	Val	Ser	Met	Asp	Leu
		515					520					525			
Ala	Thr	Phe	Met	Lys	Leu	Arg	Thr	Asp	Ala	Val	Leu	Pro	Leu	Thr	Val
		530				535					540				
Ala	Glu	Val	Gln	Lys	Leu	Leu	Gly	Pro	His	Val	Glu	Gly	Leu	Lys	Ala
545					550					555					560
Glu	Glu	Arg	His	Arg	Pro	Val	Arg	Asp	Trp	Ile	Leu	Arg	Gln	Arg	Gln
				565					570					575	
Asp	Asp	Leu	Asp	Thr	Leu	Gly	Leu	Gly	Leu	Gln	Gly	Gly	Ile	Pro	Asn
			580					585					590		
Gly	Tyr	Leu	Val	Leu	Asp	Leu	Ser	Val	Gln	Glu	Ala	Leu	Ser	Gly	Thr
		595					600					605			
Pro	Cys	Leu	Leu	Gly	Pro	Gly	Pro	Val	Leu	Thr	Val	Leu	Ala	Leu	Leu
		610				615						620			
Leu	Ala	Ser	Thr	Leu	Ala										
625					630										

&lt;210&gt; 196

&lt;211&gt; 2105

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

201

&lt;400&gt; 196

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tcctgtggga ccccgccct cggcagcctc ctgttcctgc tcttcagcct cggatgggtg 180
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&lt;210&gt; 197

&lt;211&gt; 620

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 197

```

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Ala Leu Gly Ser Leu Leu Phe Leu Leu Phe Ser Leu Gly Trp Val Gln
20          25          30
Pro Ser Arg Thr Leu Ala Gly Glu Thr Gly Gln Glu Ala Ala Pro Leu
35          40          45
Asp Gly Val Leu Ala Asn Pro Pro Asn Ile Ser Ser Leu Ser Pro Arg
50          55          60
Gln Leu Leu Gly Phe Pro Cys Ala Glu Val Ser Gly Leu Ser Thr Glu
65          70          75          80
Arg Val Arg Glu Leu Ala Val Ala Leu Ala Gln Lys Asn Val Lys Leu
85          90          95
Ser Thr Glu Gln Leu Arg Cys Leu Ala His Arg Leu Ser Glu Pro Pro
100          105          110

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202

Glu	Asp	Leu	Asp	Ala	Leu	Pro	Leu	Asp	Leu	Leu	Leu	Phe	Leu	Asn	Pro	115	120	125
Asp	Ala	Phe	Ser	Gly	Pro	Gln	Ala	Cys	Thr	Arg	Phe	Phe	Ser	Arg	Ile	130	135	140
Thr	Lys	Ala	Asn	Val	Asp	Leu	Leu	Pro	Arg	Gly	Ala	Pro	Glu	Arg	Gln	145	150	155
Arg	Leu	Leu	Pro	Ala	Ala	Leu	Ala	Cys	Trp	Gly	Val	Arg	Gly	Ser	Leu	165	170	175
Leu	Ser	Glu	Ala	Asp	Val	Arg	Ala	Leu	Gly	Gly	Leu	Ala	Cys	Asp	Leu	180	185	190
Pro	Gly	Arg	Phe	Val	Ala	Glu	Ser	Ala	Glu	Val	Leu	Leu	Pro	Arg	Leu	195	200	205
Val	Ser	Cys	Pro	Gly	Pro	Leu	Asp	Gln	Asp	Gln	Gln	Glu	Ala	Ala	Arg	210	215	220
Ala	Ala	Leu	Gln	Gly	Gly	Gly	Pro	Pro	Tyr	Gly	Pro	Pro	Ser	Thr	Trp	225	230	235
Ser	Val	Ser	Thr	Met	Asp	Ala	Leu	Arg	Gly	Leu	Leu	Pro	Val	Leu	Gly	245	250	255
Gln	Pro	Ile	Ile	Arg	Ser	Ile	Pro	Gln	Gly	Ile	Val	Ala	Ala	Trp	Arg	260	265	270
Gln	Arg	Ser	Ser	Arg	Asp	Pro	Ser	Trp	Arg	Gln	Pro	Glu	Arg	Thr	Ile	275	280	285
Leu	Arg	Pro	Arg	Phe	Arg	Arg	Glu	Val	Glu	Lys	Thr	Ala	Cys	Pro	Ser	290	295	300
Gly	Lys	Lys	Ala	Arg	Glu	Ile	Asp	Glu	Ser	Leu	Ile	Phe	Tyr	Lys	Lys	305	310	315
Trp	Glu	Leu	Glu	Ala	Cys	Val	Asp	Ala	Ala	Leu	Leu	Ala	Thr	Gln	Met	325	330	335
Asp	Arg	Val	Asn	Ala	Ile	Pro	Phe	Thr	Tyr	Glu	Gln	Leu	Asp	Val	Leu	340	345	350
Lys	His	Lys	Leu	Asp	Glu	Leu	Tyr	Pro	Gln	Gly	Tyr	Pro	Glu	Ser	Val	355	360	365
Ile	Gln	His	Leu	Gly	Tyr	Leu	Phe	Leu	Lys	Met	Ser	Pro	Glu	Asp	Ile	370	375	380
Arg	Lys	Trp	Asn	Val	Thr	Ser	Leu	Glu	Thr	Leu	Lys	Ala	Leu	Leu	Glu	385	390	395
Val	Asn	Lys	Gly	His	Glu	Met	Ser	Pro	Gln	Ala	Pro	Arg	Arg	Pro	Leu	405	410	415
Pro	Gln	Val	Ala	Thr	Leu	Ile	Asp	Arg	Phe	Val	Lys	Gly	Arg	Gly	Gln	420	425	430
Leu	Asp	Lys	Asp	Thr	Leu	Asp	Thr	Leu	Thr	Ala	Phe	Tyr	Pro	Gly	Tyr	435	440	445
Leu	Cys	Ser	Leu	Ser	Pro	Glu	Glu	Leu	Ser	Ser	Val	Pro	Pro	Ser	Ser	450	455	460
Ile	Trp	Ala	Val	Arg	Pro	Gln	Asp	Leu	Asp	Thr	Cys	Asp	Pro	Arg	Gln	465	470	475
Leu	Asp	Val	Leu	Tyr	Pro	Lys	Ala	Arg	Leu	Ala	Phe	Gln	Asn	Met	Asn	485	490	495
Gly	Ser	Glu	Tyr	Phe	Val	Lys	Ile	Gln	Ser	Phe	Leu	Gly	Gly	Ala	Pro	500	505	510
Thr	Glu	Asp	Leu	Lys	Ala	Leu	Ser	Gln	Gln	Asn	Val	Ser	Met	Asp	Leu	515	520	525
Ala	Thr	Phe	Met	Lys	Leu	Arg	Thr	Asp	Ala	Val	Leu	Pro	Leu	Thr	Val	530	535	540
Ala	Glu	Val	Gln	Lys	Leu	Leu	Gly	Pro	His	Val	Glu	Gly	Leu	Lys	Ala	545	550	555
Glu	Glu	Arg	His	Arg	Pro	Val	Arg	Asp	Trp	Ile	Leu	Arg	Gln	Arg	Gln	565	570	575

203

Asp Asp Leu Asp Thr Leu Gly Leu Gly Leu Gln Gly Gly Ile Pro Asn  
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 Gly Tyr Leu Val Leu Asp Leu Ser Val Gln Gly Pro Gly Pro Val Leu  
                   595                                  600                                  605  
 Thr Val Leu Ala Leu Leu Leu Ala Ser Thr Leu Ala  
                   610                                  615                                  620

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 <211> 2193  
 <212> DNA  
 <213> Homo sapiens

<400> 198  
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 tcctgtggga ccccgccct cggcagcctc ctgttcctgc tcttcagcct cggatgggtg 180  
 cagccctcga ggaccctggc tggagagaca gggcaggagg ctgcaccctt ggacggagtc 240  
 ctggccaacc cacctaaccat ttccagcctc tccctcgcgc aactccttgg cttcccggtg 300  
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<210> 199  
 <211> 694  
 <212> PRT  
 <213> Homo sapiens

<400> 199

204

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		20					25					30			
Pro	Ser	Arg	Thr	Leu	Ala	Gly	Glu	Thr	Gly	Gln	Glu	Ala	Ala	Pro	Leu
	35					40					45				
Asp	Gly	Val	Leu	Ala	Asn	Pro	Pro	Asn	Ile	Ser	Ser	Leu	Ser	Pro	Arg
50					55					60					
Gln	Leu	Leu	Gly	Phe	Pro	Cys	Ala	Glu	Val	Ser	Gly	Leu	Ser	Thr	Glu
65				70					75					80	
Arg	Val	Arg	Glu	Leu	Ala	Val	Ala	Leu	Ala	Gln	Lys	Asn	Val	Lys	Leu
			85					90						95	
Ser	Thr	Glu	Gln	Leu	Arg	Cys	Leu	Ala	His	Arg	Leu	Ser	Glu	Pro	Pro
		100					105						110		
Glu	Asp	Leu	Asp	Ala	Leu	Pro	Leu	Asp	Leu	Leu	Leu	Phe	Leu	Asn	Pro
	115						120					125			
Asp	Ala	Phe	Ser	Gly	Pro	Gln	Ala	Cys	Thr	Arg	Phe	Phe	Ser	Arg	Ile
130					135					140					
Thr	Lys	Ala	Asn	Val	Asp	Leu	Leu	Pro	Arg	Gly	Ala	Pro	Glu	Arg	Gln
145				150					155					160	
Arg	Leu	Leu	Pro	Ala	Ala	Leu	Ala	Cys	Trp	Gly	Val	Arg	Gly	Ser	Leu
			165					170						175	
Leu	Ser	Glu	Ala	Asp	Val	Arg	Ala	Leu	Gly	Gly	Leu	Ala	Cys	Asp	Leu
		180					185						190		
Pro	Gly	Arg	Phe	Val	Ala	Glu	Ser	Ala	Glu	Val	Leu	Leu	Pro	Arg	Leu
	195					200						205			
Val	Ser	Cys	Pro	Gly	Pro	Leu	Asp	Gln	Asp	Gln	Gln	Glu	Ala	Ala	Arg
	210					215				220					
Ala	Ala	Leu	Gln	Gly	Gly	Gly	Pro	Pro	Tyr	Gly	Pro	Pro	Ser	Thr	Trp
225				230					235						240
Ser	Val	Ser	Thr	Met	Asp	Ala	Leu	Arg	Gly	Leu	Leu	Pro	Val	Leu	Gly
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		260						265						270	
Gln	Arg	Ser	Ser	Arg	Asp	Pro	Ser	Trp	Arg	Gln	Pro	Glu	Arg	Thr	Ile
		275					280					285			
Leu	Arg	Pro	Arg	Phe	Arg	Arg	Glu	Val	Glu	Lys	Thr	Ala	Cys	Pro	Ser
	290				295						300				
Gly	Lys	Lys	Ala	Arg	Glu	Ile	Asp	Glu	Ser	Leu	Ile	Phe	Tyr	Lys	Lys
305				310					315					320	
Trp	Glu	Leu	Glu	Ala	Cys	Val	Asp	Ala	Ala	Leu	Leu	Ala	Thr	Gln	Met
			325					330						335	
Asp	Arg	Val	Asn	Ala	Ile	Pro	Phe	Thr	Tyr	Glu	Gln	Leu	Asp	Val	Leu
		340					345						350		
Lys	His	Lys	Leu	Asp	Glu	Leu	Tyr	Pro	Gln	Gly	Tyr	Pro	Glu	Ser	Val
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	370					375					380				
Arg	Lys	Trp	Asn	Val	Thr	Ser	Leu	Glu	Thr	Leu	Lys	Ala	Leu	Leu	Glu
385				390					395						400
Val	Asn	Lys	Gly	His	Glu	Met	Ser	Pro	Gln	Val	Ala	Thr	Leu	Ile	Asp
			405						410					415	
Arg	Phe	Val	Lys	Gly	Arg	Gly	Gln	Leu	Asp	Lys	Asp	Thr	Leu	Asp	Thr
		420					425						430		
Leu	Thr	Ala	Phe	Tyr	Pro	Gly	Tyr	Leu	Cys	Ser	Leu	Ser	Pro	Glu	Glu
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Leu	Ser	Ser	Val	Pro	Pro	Ser	Ser	Ile	Trp	Ala	Val	Arg	Pro	Gln	Asp
450						455					460				

205

Leu Asp Thr Cys Asp Pro Arg Gln Leu Asp Val Leu Tyr Pro Lys Ala  
 465 470 475 480  
 Arg Leu Ala Phe Gln Asn Met Asn Gly Ser Glu Tyr Phe Val Lys Ile  
 485 490 495  
 Gln Ser Phe Leu Gly Gly Ala Pro Thr Glu Asp Leu Lys Ala Leu Ser  
 500 505 510  
 Gln Gln Asn Val Ser Met Asp Leu Ala Thr Phe Met Lys Leu Arg Thr  
 515 520 525  
 Asp Ala Val Leu Pro Leu Thr Val Ala Glu Val Gln Lys Leu Leu Gly  
 530 535 540  
 Pro His Val Glu Gly Leu Lys Ala Glu Glu Arg His Arg Pro Val Arg  
 545 550 555 560  
 Asp Trp Ile Leu Arg Gln Arg Gln Asp Asp Leu Asp Thr Leu Gly Leu  
 565 570 575  
 Gly Leu Gln Gly Gly Ile Pro Asn Gly Tyr Leu Val Leu Asp Leu Ser  
 580 585 590  
 Val Gln Gly Gly Arg Gly Gly Gln Ala Arg Ala Gly Gly Arg Ala Gly  
 595 600 605  
 Gly Val Glu Val Gly Ala Leu Ser His Pro Ser Leu Cys Arg Gly Pro  
 610 615 620  
 Leu Gly Asp Ala Leu Pro Pro Arg Thr Trp Thr Cys Ser His Arg Pro  
 625 630 635 640  
 Gly Thr Ala Pro Ser Leu His Pro Gly Leu Arg Ala Pro Leu Pro Cys  
 645 650 655  
 Trp Pro Gln Pro Cys Trp Gly Ser Pro Pro Gly Gln Glu Gln Ala Arg  
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 Met Pro Pro Ala Asp Thr  
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<210> 200  
 <211> 2081  
 <212> DNA  
 <213> Homo sapiens

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 ctaaagcata aactggatga gctctaccca caaggttacc ccgagtctgt gatccagcac 1200

206

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agcgtgcaag gacctggacc tgttctcacc gtcttgccac tgctcctagc ctccacctg 1920
gcctgagggc cccactccct tgcctggccc agccctgctg gggatccccg cctggccagg 1980
agcaggcacg ggtgatcccc gttccacccc aagagaactc gcgctcagta aacgggaaca 2040
tgccccctgc agacacgtaa aaaaaaaaaa aaaaaaaaaa a 2081

```

&lt;210&gt; 201

&lt;211&gt; 612

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 201

```

Met Ala Leu Pro Thr Ala Arg Pro Leu Leu Gly Ser Cys Gly Thr Pro
  1          5          10          15
Ala Leu Gly Ser Leu Leu Phe Leu Leu Phe Ser Leu Gly Trp Val Gln
      20          25          30
Pro Ser Arg Thr Leu Ala Gly Glu Thr Gly Gln Glu Ala Ala Pro Leu
      35          40          45
Asp Gly Val Leu Ala Asn Pro Pro Asn Ile Ser Ser Leu Ser Pro Arg
      50          55          60
Gln Leu Leu Gly Phe Pro Cys Ala Glu Val Ser Gly Leu Ser Thr Glu
      65          70          75          80
Arg Val Arg Glu Leu Ala Val Ala Leu Ala Gln Lys Asn Val Lys Leu
      85          90          95
Ser Thr Glu Gln Leu Arg Cys Leu Ala His Arg Leu Ser Glu Pro Pro
      100         105         110
Glu Asp Leu Asp Ala Leu Pro Leu Asp Leu Leu Leu Phe Leu Asn Pro
      115         120         125
Asp Ala Phe Ser Gly Pro Gln Ala Cys Thr Arg Phe Phe Ser Arg Ile
      130         135         140
Thr Lys Ala Asn Val Asp Leu Leu Pro Arg Gly Ala Pro Glu Arg Gln
      145         150         155         160
Arg Leu Leu Pro Ala Ala Leu Ala Cys Trp Gly Val Arg Gly Ser Leu
      165         170         175
Leu Ser Glu Ala Asp Val Arg Ala Leu Gly Gly Leu Ala Cys Asp Leu
      180         185         190
Pro Gly Arg Phe Val Ala Glu Ser Ala Glu Val Leu Leu Pro Arg Leu
      195         200         205
Val Ser Cys Pro Gly Pro Leu Asp Gln Asp Gln Gln Glu Ala Ala Arg
      210         215         220
Ala Ala Leu Gln Gly Gly Gly Pro Pro Tyr Gly Pro Pro Ser Thr Trp
      225         230         235         240
Ser Val Ser Thr Met Asp Ala Leu Arg Gly Leu Leu Pro Val Leu Gly
      245         250         255
Gln Pro Ile Ile Arg Ser Ile Pro Gln Gly Ile Val Ala Ala Trp Arg
      260         265         270
Gln Arg Ser Ser Arg Asp Pro Ser Trp Arg Gln Pro Glu Arg Thr Ile
      275         280         285

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207

Leu Arg Pro Arg Phe Arg Arg Glu Val Glu Lys Thr Ala Cys Pro Ser  
 290 295 300  
 Gly Lys Lys Ala Arg Glu Ile Asp Glu Ser Leu Ile Phe Tyr Lys Lys  
 305 310 315 320  
 Trp Glu Leu Glu Ala Cys Val Asp Ala Ala Leu Leu Ala Thr Gln Met  
 325 330 335  
 Asp Arg Val Asn Ala Ile Pro Phe Thr Tyr Glu Gln Leu Asp Val Leu  
 340 345 350  
 Lys His Lys Leu Asp Glu Leu Tyr Pro Gln Gly Tyr Pro Glu Ser Val  
 355 360 365  
 Ile Gln His Leu Gly Tyr Leu Phe Leu Lys Met Ser Pro Glu Asp Ile  
 370 375 380  
 Arg Lys Trp Asn Val Thr Ser Leu Glu Thr Leu Lys Ala Leu Leu Glu  
 385 390 395 400  
 Val Asn Lys Gly His Glu Met Ser Pro Gln Val Ala Thr Leu Ile Asp  
 405 410 415  
 Arg Phe Val Lys Gly Arg Gly Gln Leu Asp Lys Asp Thr Leu Asp Thr  
 420 425 430  
 Leu Thr Ala Phe Tyr Pro Gly Tyr Leu Cys Ser Leu Ser Pro Glu Glu  
 435 440 445  
 Leu Ser Ser Val Pro Pro Ser Ser Ile Trp Ala Val Arg Pro Gln Asp  
 450 455 460  
 Leu Asp Thr Cys Asp Pro Arg Gln Leu Asp Val Leu Tyr Pro Lys Ala  
 465 470 475 480  
 Arg Leu Ala Phe Gln Asn Met Asn Gly Ser Glu Tyr Phe Val Lys Ile  
 485 490 495  
 Gln Ser Phe Leu Gly Gly Ala Pro Thr Glu Asp Leu Lys Ala Leu Ser  
 500 505 510  
 Gln Gln Asn Val Ser Met Asp Leu Ala Thr Phe Met Lys Leu Arg Thr  
 515 520 525  
 Asp Ala Val Leu Pro Leu Thr Val Ala Glu Val Gln Lys Leu Leu Gly  
 530 535 540  
 Pro His Val Glu Gly Leu Lys Ala Glu Glu Arg His Arg Pro Val Arg  
 545 550 555 560  
 Asp Trp Ile Leu Arg Gln Arg Gln Asp Asp Leu Asp Thr Leu Gly Leu  
 565 570 575  
 Gly Leu Gln Gly Gly Ile Pro Asn Gly Tyr Leu Val Leu Asp Leu Ser  
 580 585 590  
 Val Gln Gly Pro Gly Pro Val Leu Thr Val Leu Ala Leu Leu Leu Ala  
 595 600 605  
 Ser Thr Leu Ala  
 610

&lt;210&gt; 202

&lt;211&gt; 1195

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 202

gtggagaaga cagcctgtcc ttcaggcaag aaggcccgcg agatagacga gagcctcatc 60  
 ttctacaaga agtgggagct ggaagcctgc gtggatgcgg ccctgtctggc caccagatg 120  
 gaccgcgtga acgccatccc cttcacctac gagcagctgg acgtcctaaa gcataaactg 180  
 gatgagctct acccacaagg ttaccctgag tctgtgatcc agcacctggg ctacctcttc 240  
 ctcaagatga gccctgagga cattcgcaag tggaatgtga cgtccctgga gacctgaag 300  
 gctttgcttg aagtcaaca agggcacgaa atgagtcctc aggtggccac cctgatcgac 360  
 cgctttgtga agggaagggg ccagctagac aaagacacc tagacaccct gaccgccttc 420  
 taccctgggt acctgtgtc cctcagcccc gaggagctga gctccgtgcc cccagcagc 480

208

```

atctgggcg ttagggccca ggacctggac acgtgtgacc caaggcagct ggacgtcctc 540
tatcccaagg cccgccttgc tttccagaac atgaacgggt ccgaatactt cgtgaagatc 600
cagtccttcc tgggtggggc cccacaggag gatttgaagg cgctcagtca gcagaatgtg 660
agcatggact tggccacgtt catgaagctg cggacggatg cgggtgctgcc gttgactgtg 720
gctgaggtgc agaaacttct gggacccac gtggagggcc tgaaggcgga ggagcggcac 780
cgcccggtgc gggactggat cctacggcag cggcaggacg acctggacac gctggggctg 840
gggctacagg gcggcatccc caacggctac ctggtcctag acctcagcgt gcaaggtggg 900
cggggcggcc aggccagggc tgggggcaga gctgggggcg tggaggtggg cgctctgagt 960
caccctctc tctgtagagg ccctctcggg gacgccctgc ctctaggac ctggacctgt 1020
tctcaccgtc ctggcactgc tcctagcctc caccctggcc tgaggggccc actcccttgc 1080
tggccccagc cctgctgggg atccccgcct ggccaggagc aggcacgggt gatccccgtt 1140
ccacccaag agaactcgcg ctcatgaaac ggaacatgc cccctgcaga cacgt 1195

```

&lt;210&gt; 203

&lt;211&gt; 398

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 203

```

Val Glu Lys Thr Ala Cys Pro Ser Gly Lys Lys Ala Arg Glu Ile Asp
 1          5          10          15
Glu Ser Leu Ile Phe Tyr Lys Lys Trp Glu Leu Glu Ala Cys Val Asp
 20          25          30
Ala Ala Leu Leu Ala Thr Gln Met Asp Arg Val Asn Ala Ile Pro Phe
 35          40          45
Thr Tyr Glu Gln Leu Asp Val Leu Lys His Lys Leu Asp Glu Leu Tyr
 50          55          60
Pro Gln Gly Tyr Pro Glu Ser Val Ile Gln His Leu Gly Tyr Leu Phe
 65          70          75          80
Leu Lys Met Ser Pro Glu Asp Ile Arg Lys Trp Asn Val Thr Ser Leu
 85          90          95
Glu Thr Leu Lys Ala Leu Leu Glu Val Asn Lys Gly His Glu Met Ser
100          105          110
Pro Gln Val Ala Thr Leu Ile Asp Arg Phe Val Lys Gly Arg Gly Gln
115          120          125
Leu Asp Lys Asp Thr Leu Asp Thr Leu Thr Ala Phe Tyr Pro Gly Tyr
130          135          140
Leu Cys Ser Leu Ser Pro Glu Glu Leu Ser Ser Val Pro Pro Ser Ser
145          150          155          160
Ile Trp Ala Val Arg Pro Gln Asp Leu Asp Thr Cys Asp Pro Arg Gln
165          170          175
Leu Asp Val Leu Tyr Pro Lys Ala Arg Leu Ala Phe Gln Asn Met Asn
180          185          190
Gly Ser Glu Tyr Phe Val Lys Ile Gln Ser Phe Leu Gly Gly Ala Pro
195          200          205
Thr Glu Asp Leu Lys Ala Leu Ser Gln Gln Asn Val Ser Met Asp Leu
210          215          220
Ala Thr Phe Met Lys Leu Arg Thr Asp Ala Val Leu Pro Leu Thr Val
225          230          235          240
Ala Glu Val Gln Lys Leu Leu Gly Pro His Val Glu Gly Leu Lys Ala
245          250          255
Glu Glu Arg His Arg Pro Val Arg Asp Trp Ile Leu Arg Gln Arg Gln
260          265          270
Asp Asp Leu Asp Thr Leu Gly Leu Gly Leu Gln Gly Gly Ile Pro Asn
275          280          285
Gly Tyr Leu Val Leu Asp Leu Ser Val Gln Gly Gly Arg Gly Gly Gln
290          295          300
Ala Arg Ala Gly Gly Arg Ala Gly Gly Val Glu Val Gly Ala Leu Ser

```

209

305					310					315				320
His	Pro	Ser	Leu	Cys	Arg	Gly	Pro	Leu	Gly	Asp	Ala	Leu	Pro	Pro Arg
				325					330					335
Thr	Trp	Thr	Cys	Ser	His	Arg	Pro	Gly	Thr	Ala	Pro	Ser	Leu	His Pro
			340					345					350	
Gly	Leu	Arg	Ala	Pro	Leu	Pro	Cys	Trp	Pro	Gln	Pro	Cys	Trp	Gly Ser
		355					360					365		
Pro	Pro	Gly	Gln	Glu	Gln	Ala	Arg	Val	Ile	Pro	Val	Pro	Pro	Gln Glu
	370					375					380			
Asn	Ser	Arg	Ser	Val	Asn	Gly	Asn	Met	Pro	Pro	Ala	Asp	Thr	
385					390					395				

&lt;210&gt; 204

&lt;211&gt; 2085

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 204

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ccctccctgg	gatctacaca	gaccatggcc	ttgccaacgg	ctcgaccctt	gttgggggtcc	120
tgtgggaccc	ccgccctcgg	cagcctcctg	ttcctgctct	tcagcctcgg	atgggtgcag	180
ccctcgagga	ccctggctgg	agagacaggg	caggaggctg	cacccctgga	cggagtccctg	240
gccaacccac	ctaacatttc	cagcctctcc	cctcgccaac	tccttggctt	cccgtgtgcg	300
gaggtgtccg	gcctgagcac	ggagcgtgtc	cgaggagctg	ctgtggcctt	ggcacagaag	360
aatgtcaagc	tctcaacaga	gcagctgcgc	tgtctggctc	accggctctc	tgagccccc	420
gaggacctgg	acgccctccc	attggacctg	ctgctattcc	tcaaccacga	tgcgttctcg	480
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cgggggtctc	tgctgagcga	ggctgatgtg	cgggctctgg	gaggcctggc	ttgcgacctg	660
cctgggcgct	ttgtggccga	gtcggccgaa	gtgctgctac	cccggctggt	gagctgcccc	720
ggacccctgg	accaggacca	gcaggaggca	gccagggcgg	ctctgcaggg	cgggggaccc	780
ccctacggcc	ccccgtcgac	atggtctgtc	tccacgatgg	acgctctgcg	gggcctgctg	840
cccgctgctg	gccagcccat	catccgcagc	atcccgagg	gcctcgtggc	cgcgtggcgg	900
caacgctcct	ctcgggaccc	atcctggcgg	cagcctgaac	ggaccatcct	ccggccgagg	960
ttccggcggg	aagtggagaa	gacagcctgt	ccttcaggca	agaaggcccc	cgagatagac	1020
gagagcctca	tcttctacaa	gaagtgggag	ctggaagcct	gcgtggatgc	ggccctgctg	1080
gccacccaaga	tggaccgcgt	gaacgccatc	cccttcacct	acgagcagct	ggacgtccta	1140
aagcataaac	tggatgagct	ctaccacaaa	ggttaccocg	agtctgtgat	ccagcacctg	1200
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ccccccagca	gcattctggc	ggtcaggccc	caggacctgg	acacgtgtga	cccaaggcag	1500
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cagcagaatg	tgagcatgga	cttggccacg	ttcatgaagc	tgccggacga	tgcggtgctg	1680
ccgttgactg	tggctgaggt	gcagaaaactt	ctgggacccc	acgtggaggg	cctgaaggcg	1740
gaggagcggc	accgcccggg	gcgggactgg	atcctacggc	agcggcagga	cgacctggac	1800
acgtctgggc	tggggttaca	gggcggcatc	cccaacggct	acctggctcct	agacctcagc	1860
gtgcaagagg	ccctctcggg	gacgccctgc	ctcctaggac	ctggacctgt	tctcaccgtc	1920
ctggcactgc	tcttagcctc	caccctggcc	tgaggggccc	actcccttgc	tgggcccagc	1980
cctgctgggg	atccccgcct	ggccaggagc	aggcacgggt	gatccccgtt	ccaccccaag	2040
agaactcgcg	ctcagtaaac	gggaacatgc	cccctgcaga	cacgt		2085

&lt;210&gt; 205

&lt;211&gt; 622

&lt;212&gt; PRT

210

&lt;213&gt; Homo sapiens

&lt;400&gt; 205

```

Met Ala Leu Pro Thr Ala Arg Pro Leu Leu Gly Ser Cys Gly Thr Pro
 1          5          10          15
Ala Leu Gly Ser Leu Leu Phe Leu Leu Phe Ser Leu Gly Trp Val Gln
 20          25          30
Pro Ser Arg Thr Leu Ala Gly Glu Thr Gly Gln Glu Ala Ala Pro Leu
 35          40          45
Asp Gly Val Leu Ala Asn Pro Pro Asn Ile Ser Ser Leu Ser Pro Arg
 50          55          60
Gln Leu Leu Gly Phe Pro Cys Ala Glu Val Ser Gly Leu Ser Thr Glu
 65          70          75          80
Arg Val Arg Glu Leu Ala Val Ala Leu Ala Gln Lys Asn Val Lys Leu
 85          90          95
Ser Thr Glu Gln Leu Arg Cys Leu Ala His Arg Leu Ser Glu Pro Pro
 100          105          110
Glu Asp Leu Asp Ala Leu Pro Leu Asp Leu Leu Leu Phe Leu Asn Pro
 115          120          125
Asp Ala Phe Ser Gly Pro Gln Ala Cys Thr Arg Phe Phe Ser Arg Ile
 130          135          140
Thr Lys Ala Asn Val Asp Leu Leu Pro Arg Gly Ala Pro Glu Arg Gln
 145          150          155          160
Arg Leu Leu Pro Ala Ala Leu Ala Cys Trp Gly Val Arg Gly Ser Leu
 165          170          175
Leu Ser Glu Ala Asp Val Arg Ala Leu Gly Gly Leu Ala Cys Asp Leu
 180          185          190
Pro Gly Arg Phe Val Ala Glu Ser Ala Glu Val Leu Leu Pro Arg Leu
 195          200          205
Val Ser Cys Pro Gly Pro Leu Asp Gln Asp Gln Gln Glu Ala Ala Arg
 210          215          220
Ala Ala Leu Gln Gly Gly Gly Pro Pro Tyr Gly Pro Pro Ser Thr Trp
 225          230          235          240
Ser Val Ser Thr Met Asp Ala Leu Arg Gly Leu Leu Pro Val Leu Gly
 245          250          255
Gln Pro Ile Ile Arg Ser Ile Pro Gln Gly Ile Val Ala Ala Trp Arg
 260          265          270
Gln Arg Ser Ser Arg Asp Pro Ser Trp Arg Gln Pro Glu Arg Thr Ile
 275          280          285
Leu Arg Pro Arg Phe Arg Arg Glu Val Glu Lys Thr Ala Cys Pro Ser
 290          295          300
Gly Lys Lys Ala Arg Glu Ile Asp Glu Ser Leu Ile Phe Tyr Lys Lys
 305          310          315          320
Trp Glu Leu Glu Ala Cys Val Asp Ala Ala Leu Leu Ala Thr Gln Met
 325          330          335
Asp Arg Val Asn Ala Ile Pro Phe Thr Tyr Glu Gln Leu Asp Val Leu
 340          345          350
Lys His Lys Leu Asp Glu Leu Tyr Pro Gln Gly Tyr Pro Glu Ser Val
 355          360          365
Ile Gln His Leu Gly Tyr Leu Phe Leu Lys Met Ser Pro Glu Asp Ile
 370          375          380
Arg Lys Trp Asn Val Thr Ser Leu Glu Thr Leu Lys Ala Leu Leu Glu
 385          390          395          400
Val Asn Lys Gly His Glu Met Ser Pro Gln Val Ala Thr Leu Ile Asp
 405          410          415
Arg Phe Val Lys Gly Arg Gly Gln Leu Asp Lys Asp Thr Leu Asp Thr
 420          425          430
Leu Thr Ala Phe Tyr Pro Gly Tyr Leu Cys Ser Leu Ser Pro Glu Glu

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211

435	440	445
Leu Ser Ser Val Pro Pro Ser Ser Ile Trp Ala Val Arg Pro Gln Asp		
450	455	460
Leu Asp Thr Cys Asp Pro Arg Gln Leu Asp Val Leu Tyr Pro Lys Ala		
465	470	475
Arg Leu Ala Phe Gln Asn Met Asn Gly Ser Glu Tyr Phe Val Lys Ile		
485	490	495
Gln Ser Phe Leu Gly Gly Ala Pro Thr Glu Asp Leu Lys Ala Leu Ser		
500	505	510
Gln Gln Asn Val Ser Met Asp Leu Ala Thr Phe Met Lys Leu Arg Thr		
515	520	525
Asp Ala Val Leu Pro Leu Thr Val Ala Glu Val Gln Lys Leu Leu Gly		
530	535	540
Pro His Val Glu Gly Leu Lys Ala Glu Glu Arg His Arg Pro Val Arg		
545	550	555
Asp Trp Ile Leu Arg Gln Arg Gln Asp Asp Leu Asp Thr Leu Gly Leu		
565	570	575
Gly Leu Gln Gly Gly Ile Pro Asn Gly Tyr Leu Val Leu Asp Leu Ser		
580	585	590
Val Gln Glu Ala Leu Ser Gly Thr Pro Cys Leu Leu Gly Pro Gly Pro		
595	600	605
Val Leu Thr Val Leu Ala Leu Leu Leu Ala Ser Thr Leu Ala		
610	615	620

<210> 206  
 <211> 2111  
 <212> DNA  
 <213> Homo sapiens

<400> 206  
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 cctccctccc tgggatctac acagaccatg gccttgccaa cggctcgacc cctggtgggg 120  
 tcctgtggga ccccgccct cggcagcctc ctgttcctgc tcttcagcct cggatgggtg 180  
 cagccctcga ggaccctggc tggagagaca gggcaggagg ctgcaccctt ggacggagtc 240  
 ctggccaacc cacctaaccat ttccagcctc tccctcgcgc aactccttgg cttcccggtg 300  
 gcggaggtgt ccggcctgag cacggagcgt gtccgggagc tggctgtggc cttggcacag 360  
 aagaatgtca agctctcaac agagcagctg cgctgtctgg ctacccggct ctctgagccc 420  
 cccgaggacc tggacgccct cccattggac ctgctgctat tctcaaccc agatgcgttc 480  
 tcggggcccc aggcctgcac ccgtttcttc tcccgcatca cgaaggccaa tgtggacctg 540  
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 gtgcgggggt ctctgctgag cgaggctgat gtgcgggctc tgggaggcct ggcttgcgac 660  
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 ccgggacccc tggaccagga ccagcaggag gcagccaggg cggctctgca gggcggggga 780  
 cccccctacg gccccccgtc gacatggtct gtctccacga tggacgctct gcggggcctg 840  
 ctgcccgtgc tgggccagcc catcatccgc agcatccgc agggcatcgt ggccgcgtg 900  
 cggcaacgct cctctcgga ccatcctg cggcagcctg aacggaccat cctccggccg 960  
 cggttccggc ggggaagtga gaagacagcc tgtccttcag gcaagaaggc ccgcgagata 1020  
 gacgagagcc tcatcttcta caagaagtgg gagctggaag cctgcgtgga tgcggccctg 1080  
 ctggccaacc agatggaccg cgtgaacgcc atccccttca cctacgagca gctggacgtc 1140  
 ctaaagcata aactggatga gctctacca caaggttacc ccgagctctg gatccagcac 1200  
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 accctgacgc ctttctaccc tgggtacctg tctccctca gccccagga gctgagctcc 1440  
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 cagctggacg tctctatcc caaggccgc cttgctttcc agaacatgaa cgggtccgaa 1560  
 tacttcgtga agatccagtc cttcctgggt ggggccccca cggaggattt gaaggcgctc 1620

212

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agtcagcaga atgtgagcat ggacttggcc acgttcatga agctgcgga ggatgcggtg 1680
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gcgaggagac ggcaccgccc ggtgcgggac tggatcctac ggcagcgga ggacgacctg 1800
gacacgctgg ggctggggct acagggcggc atccccaacg gctacctggt cctagacctc 1860
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agccctgtcg gggatccccg cctggccagg agcaggcacg ggtgatcccc gttccacccc 2040
aagagaactc gcgctcagta aacgggaaca tgccccctgc agacacgtaa aaaaaaaaaa 2100
aaaaaaaaa a                                     2111

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&lt;210&gt; 207

&lt;211&gt; 2107

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 207

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gcctccctcc ctgggatcta cacagaccat ggccttgcaa cggctcgacc cctgttggtc 120
ctgtggggac cgccctggca gctcctgtt cctgctcttc agcctcgga ggtgcatcc 180
cgcgaggacc ctggctggag agacagggac ggagtctgcc cccctggggg gagtctgac 240
aaccgcccat aacatttcca gcctctcccc tgccaaactc cttggcttcc cgtgtcgga 300
ggtgtccggc ctgagcacgg agcgtgtccg ggagctggct gtggccttg cacagaaga 360
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ggacctggac gccctcccat tggacctgct gctattcctc aaccagatg cgttctcggg 480
gccccaggcc tgcaccggtt tcttctcccc catcacgaag gccaatgtgg acctgctccc 540
gaggggggct cccgagcgac agcggctgct gcctgcggtc ctggcctgct ggggtgtgag 600
ggggctctct ctgagcgagg ctgatgtgag ggccttgga ggcctggctt gcgacctgcc 660
tgggcgcttt gtggccgagt cggccgaagt gctgctacc cggctgggtg gctgcccggg 720
accctggac caggaccagc aggaggcagc caggcgcgct ctgcaggcg ggggaccccc 780
ctacggcccc ccgtcgacat ggtctgtctc cagcatggac gctctgcggg gcctgctgcc 840
cgtgctgggc cagcccatca tccgcagcat cccgcagggc atcgtggccg cgtggcgga 900
acgtcctctc cgggacccat cctggcgga gcctgaacgg accatcctcc ggccgcggtt 960
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gcggccccct ccacagggtg ccaccctgat cgaccgcttt gtgaaggga ggggccagct 1380
agacaaagac accctagaca cctgaccgc cttctaccct gggtagctgt gctccctcag 1440
ccccgaggag ctgagctccg tgccccccag cagcatctgg gcggtcaggc cccaggacct 1500
ggacacgtgt gacccaaggc agctggacgt cctctatccc aaggcccgcc ttgctttcca 1560
gaacatgaac gggctccgaat acttcgtgaa gatccagtcc ttcctgggtg gggccccac 1620
ggaggatttg aaggcgctca gtcagcagaa tgtgagcatg gacttggcca cgttcatgaa 1680
gctgcggacg gatgcggtgc tgccgttgac tgtggctgag gtgcagaaac ttctgggacc 1740
ccacgtggag ggcctgaagg cggaggagcg gcaccgccc gtgcgggact ggatcctacg 1800
gcagcggcag gacgacctgg acacgctggg gctggggcta caggcgga tccccaacgg 1860
ctacctggtc ctagacctca gcgtgcaaga gaccctctcg gggacgccct gcctcctagg 1920
acctggacct gttctcaccg tccctggact gctcctagcc tccaccctgg cctgaggggc 1980
ccactccctt gctggcccca gcctgctgg ggtatccccg ctggccagga gcaggcacgg 2040
gtgatccccg ttccacccca agagaactcg cgctcagtaa acgggaacat gccccctgca 2100
gacacgt                                     2107

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&lt;210&gt; 208

&lt;211&gt; 628

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

213

&lt;400&gt; 208

```

Met Ala Leu Gln Arg Leu Asp Pro Cys Trp Ser Cys Gly Asp Arg Pro
 1          5          10          15
Gly Ser Leu Leu Phe Leu Leu Phe Ser Leu Gly Trp Val His Pro Ala
          20          25          30
Arg Thr Leu Ala Gly Glu Thr Gly Thr Glu Ser Ala Pro Leu Gly Gly
          35          40          45
Val Leu Thr Thr Pro His Asn Ile Ser Ser Leu Ser Pro Arg Gln Leu
          50          55          60
Leu Gly Phe Pro Cys Ala Glu Val Ser Gly Leu Ser Thr Glu Arg Val
65          70          75          80
Arg Glu Leu Ala Val Ala Leu Ala Gln Lys Asn Val Lys Leu Ser Thr
          85          90          95
Glu Gln Leu Arg Cys Leu Ala His Arg Leu Ser Glu Pro Pro Glu Asp
          100          105          110
Leu Asp Ala Leu Pro Leu Asp Leu Leu Leu Phe Leu Asn Pro Asp Ala
          115          120          125
Phe Ser Gly Pro Gln Ala Cys Thr Arg Phe Phe Ser Arg Ile Thr Lys
130          135          140
Ala Asn Val Asp Leu Leu Pro Arg Gly Ala Pro Glu Arg Gln Arg Leu
145          150          155          160
Leu Pro Ala Ala Leu Ala Cys Trp Gly Val Arg Gly Ser Leu Leu Ser
          165          170          175
Glu Ala Asp Val Arg Ala Leu Gly Gly Leu Ala Cys Asp Leu Pro Gly
          180          185          190
Arg Phe Val Ala Glu Ser Ala Glu Val Leu Leu Pro Arg Leu Val Ser
          195          200          205
Cys Pro Gly Pro Leu Asp Gln Asp Gln Gln Glu Ala Ala Arg Ala Ala
210          215          220
Leu Gln Gly Gly Gly Pro Pro Tyr Gly Pro Pro Ser Thr Trp Ser Val
225          230          235          240
Ser Thr Met Asp Ala Leu Arg Gly Leu Leu Pro Val Leu Gly Gln Pro
          245          250          255
Ile Ile Arg Ser Ile Pro Gln Gly Ile Val Ala Ala Trp Arg Gln Arg
          260          265          270
Ser Ser Arg Asp Pro Ser Trp Arg Gln Pro Glu Arg Thr Ile Leu Arg
          275          280          285
Pro Arg Phe Arg Arg Glu Val Glu Lys Thr Ala Cys Pro Ser Gly Lys
290          295          300
Lys Ala Arg Glu Ile Asp Glu Ser Leu Ile Phe Tyr Lys Lys Trp Glu
305          310          315          320
Leu Glu Ala Cys Val Asp Ala Ala Leu Leu Ala Thr Gln Met Asp Arg
          325          330          335
Val Asn Ala Ile Pro Phe Thr Tyr Glu Gln Leu Asp Val Leu Lys His
          340          345          350
Lys Leu Asp Glu Leu Tyr Pro Gln Gly Tyr Pro Glu Ser Val Ile Gln
          355          360          365
His Leu Gly Tyr Leu Phe Leu Lys Met Ser Pro Glu Asp Ile Arg Lys
370          375          380
Trp Asn Val Thr Ser Leu Glu Thr Leu Lys Ala Leu Leu Glu Val Asp
385          390          395          400
Lys Gly His Glu Met Ser Pro Gln Ala Pro Arg Arg Pro Leu Pro Gln
          405          410          415
Val Ala Thr Leu Ile Asp Arg Phe Val Lys Gly Arg Gly Gln Leu Asp
          420          425          430
Lys Asp Thr Leu Asp Thr Leu Thr Ala Phe Tyr Pro Gly Tyr Leu Cys
          435          440          445
Ser Leu Ser Pro Glu Glu Leu Ser Ser Val Pro Pro Ser Ser Ile Trp

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214

450	455	460
Ala Val Arg Pro Gln Asp	Leu Asp Thr Cys Asp	Pro Arg Gln Leu Asp
465	470	475
Val Leu Tyr Pro Lys Ala Arg Leu Ala Phe Gln	Asn Met Asn Gly Ser	480
	485	490
Glu Tyr Phe Val Lys Ile Gln Ser Phe Leu Gly Gly Ala Pro Thr Glu		495
	500	505
Asp Leu Lys Ala Leu Ser Gln Gln Asn Val Ser Met Asp Leu Ala Thr		510
	515	520
Phe Met Lys Leu Arg Thr Asp Ala Val Leu Pro Leu Thr Val Ala Glu		525
	530	535
Val Gln Lys Leu Leu Gly Pro His Val Glu Gly Leu Lys Ala Glu Glu		540
545	550	555
Arg His Arg Pro Val Arg Asp Trp Ile Leu Arg Gln Arg Gln Asp Asp		560
	565	570
Leu Asp Thr Leu Gly Leu Gly Leu Gln Gly Gly Ile Pro Asn Gly Tyr		575
	580	585
Leu Val Leu Asp Leu Ser Val Gln Glu Thr Leu Ser Gly Thr Pro Cys		590
	595	600
Leu Leu Gly Pro Gly Pro Val Leu Thr Val Leu Ala Leu Leu Leu Ala		605
610	615	620
Ser Thr Leu Ala		
625		

&lt;210&gt; 209

&lt;211&gt; 2316

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 209

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ctatagggag tcgacccacg cgctccgccg gcgttagggg taaagctccc tacccaactg 60
cgcagaaggc ctcaagaggc tgggggctgg gcttcccctt tcacatcgcc ctttagaggc 120
ccacgtgtgg gcattggccs gcgatctgaa aggggctgtc ctgttcctca tgggcgctgc 180
cagcgccacg cactcctctt tctgcctggc cggccactcc cgtctgctgt gacgcgcgga 240
cagagagcta ccggtggacc cagcgtgcct ccctccctgg gatctacaca gaccatggcc 300
ttgccaaagg ctcgaccctt gttggggctc tgtgggaccc ccgccctcgg cagcctcctg 360
ttcctgctct tcagcctcgg atgggtgcag ccctcgagga ccctggctgg agagacaggg 420
caggaggetg cgcccctgga cggagtcctg gccaaacccac ctaacatttc cagcctctcc 480
cctcgccaac tccttggett cccgtgtgag gaggtgtccg gcctgagcac ggagcgtgtc 540
cgggagctgg ctgtggcctt ggcacagaag aatgtcaagc tctcaacaga gcagctgcgc 600
tgtctggctc accggctctc tgagccccc gaggacctgg acgccctccc attggacctg 660
ctgctattcc tyaacccaga tgcgttctcg gggccccagg cctgcacccg tttcttctcc 720
cgcatacaga aggccaatgt ggacctgtc cggagggggg ctcccagcg acagcggctg 780
ctgcctgcgg ctctggcctg ctgggggtgt cgggggtctc tgetgagcga ggctgatgtg 840
cgggctctgg gaggcctggc ttgcgacctg cctgggcgct ttgtggccga gtcggccgaa 900
gtgctgtac ccggctgggt gagctgccg ggacccttg accaggacca gcaggaggca 960
gccagggcgg ctctgcagg cgggggaccc ccctacggc cccgctcgac atggtctgtc 1020
tccacgatgg acgetctgcg gggcctgtg cccgtgctgg gccagcccat catccgcagc 1080
atccgcagg gcctcgtggc cgcgtggcgg caacgctcct ctcgggaccc atcctggcgg 1140
cagcctgaac ggaccatcct ccggccgcgg ttccggcggg aagtggagaa gacagcctgt 1200
ccttcaggca agaaggccc cgagatagac gagagcctca tcttctacaa gaagtgggag 1260
ctggaagcct gcgtggatgc ggccctgtg gccaccaga tggaccgct gaacgccatc 1320
cccttcacct acgagcagct ggacgtccta aagcataaac tggatgagct ctaccacaa 1380
ggttaccocg agtctgtgat ccagcacctg ggctacctt tctcaagat gagcctgag 1440
gacattcgca agtggaaatg gacgtccctg gagaccctga aggctttgt tgaagtcgac 1500
aaagggcacg aaatgagtc tcaggctcct cggcgccccc tccacaggt ggccaccctg 1560
atcgaccgct ttgtgaaggg aaggggccag ctagacaaa acaccctaga caccctgacc 1620

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215

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gccttctacc ctgggtacct gtgctccctc agccccgagg agctgagctc cgtgcccccc 1680
agcagcatct gggcggtcag gccccaggac ctggacacgt gtgaccacaag gcagctggac 1740
gtcctctatc ccaaggcccg ccttgctttc cagaacatga acgggtccga atacttcgtg 1800
aagatccagt ccttctctggg tggggccccc acggaggatt tgaaggcgct cagtcagcag 1860
aatgtgagca tggacttggc cacgttcacg aagctgcgga cggatgcggt gctgccgttg 1920
actgtggctg aggtgcagaa acttctggga cccacagtgg agggcctgaa ggcggaggag 1980
cggcaccgcc cgggtgcgga ctggatccta cggcagcggc aggacgacct ggacacgctg 2040
gggctggggc tacagggcgg catccccaac ggctacctgg tcctagacct cagcgtgcaa 2100
gasrcctct cggggacgcc ctgcctccta ggacctggac ctgttctcac cgtcctggca 2160
ctgctcctag cctccaccct ggcctgaggg cccactccc ttgctggccc cagccctgct 2220
ggggatcccc gcctggccag gaggaggcac gggtgatccc cgttccaccc caagagaact 2280
cgcgctcagt aaacgggaac atgccccctg cagaca 2316

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&lt;210&gt; 210

&lt;211&gt; 630

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; VARIANT

&lt;222&gt; (1) ... (630)

&lt;223&gt; Xaa = Any Amino Acid

&lt;400&gt; 210

```

Met Ala Leu Pro Thr Ala Arg Pro Leu Leu Gly Ser Cys Gly Thr Pro
1      5      10      15
Ala Leu Gly Ser Leu Leu Phe Leu Leu Phe Ser Leu Gly Trp Val Gln
20     25     30
Pro Ser Arg Thr Leu Ala Gly Glu Thr Gly Gln Glu Ala Ala Pro Leu
35     40     45
Asp Gly Val Leu Ala Asn Pro Asn Ile Ser Ser Leu Ser Pro Arg
50     55     60
Gln Leu Leu Gly Phe Pro Cys Ala Glu Val Ser Gly Leu Ser Thr Glu
65     70     75     80
Arg Val Arg Glu Leu Ala Val Ala Leu Ala Gln Lys Asn Val Lys Leu
85     90     95
Ser Thr Glu Gln Leu Arg Cys Leu Ala His Arg Leu Ser Glu Pro Pro
100    105    110
Glu Asp Leu Asp Ala Leu Pro Leu Asp Leu Leu Leu Phe Leu Asn Pro
115    120    125
Asp Ala Phe Ser Gly Pro Gln Ala Cys Thr Arg Phe Phe Ser Arg Ile
130    135    140
Thr Lys Ala Asn Val Asp Leu Leu Pro Arg Gly Ala Pro Glu Arg Gln
145    150    155    160
Arg Leu Leu Pro Ala Ala Leu Ala Cys Trp Gly Val Arg Gly Ser Leu
165    170    175
Leu Ser Glu Ala Asp Val Arg Ala Leu Gly Gly Leu Ala Cys Asp Leu
180    185    190
Pro Gly Arg Phe Val Ala Glu Ser Ala Glu Val Leu Leu Pro Arg Leu
195    200    205
Val Ser Cys Pro Gly Pro Leu Asp Gln Asp Gln Gln Glu Ala Ala Arg
210    215    220
Ala Ala Leu Gln Gly Gly Gly Pro Pro Tyr Gly Pro Pro Ser Thr Trp
225    230    235    240
Ser Val Ser Thr Met Asp Ala Leu Arg Gly Leu Leu Pro Val Leu Gly
245    250    255
Gln Pro Ile Ile Arg Ser Ile Pro Gln Gly Ile Val Ala Ala Trp Arg
260    265    270

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216

Gln Arg Ser Ser Arg Asp Pro Ser Trp Arg Gln Pro Glu Arg Thr Ile  
           275                          280                          285  
 Leu Arg Pro Arg Phe Arg Arg Glu Val Glu Lys Thr Ala Cys Pro Ser  
           290                          295                          300  
 Gly Lys Lys Ala Arg Glu Ile Asp Glu Ser Leu Ile Phe Tyr Lys Lys  
 305                          310                          315                          320  
 Trp Glu Leu Glu Ala Cys Val Asp Ala Ala Leu Leu Ala Thr Gln Met  
                           325                          330                          335  
 Asp Arg Val Asn Ala Ile Pro Phe Thr Tyr Glu Gln Leu Asp Val Leu  
                           340                          345                          350  
 Lys His Lys Leu Asp Glu Leu Tyr Pro Gln Gly Tyr Pro Glu Ser Val  
                           355                          360                          365  
 Ile Gln His Leu Gly Tyr Leu Phe Leu Lys Met Ser Pro Glu Asp Ile  
           370                          375                          380  
 Arg Lys Trp Asn Val Thr Ser Leu Glu Thr Leu Lys Ala Leu Leu Glu  
 385                          390                          395                          400  
 Val Asp Lys Gly His Glu Met Ser Pro Gln Ala Pro Arg Arg Pro Leu  
                           405                          410                          415  
 Pro Gln Val Ala Thr Leu Ile Asp Arg Phe Val Lys Gly Arg Gly Gln  
                           420                          425                          430  
 Leu Asp Lys Asp Thr Leu Asp Thr Leu Thr Ala Phe Tyr Pro Gly Tyr  
                           435                          440                          445  
 Leu Cys Ser Leu Ser Pro Glu Glu Leu Ser Ser Val Pro Pro Ser Ser  
                           450                          455                          460  
 Ile Trp Ala Val Arg Pro Gln Asp Leu Asp Thr Cys Asp Pro Arg Gln  
 465                          470                          475                          480  
 Leu Asp Val Leu Tyr Pro Lys Ala Arg Leu Ala Phe Gln Asn Met Asn  
                           485                          490                          495  
 Gly Ser Glu Tyr Phe Val Lys Ile Gln Ser Phe Leu Gly Gly Ala Pro  
                           500                          505                          510  
 Thr Glu Asp Leu Lys Ala Leu Ser Gln Gln Asn Val Ser Met Asp Leu  
                           515                          520                          525  
 Ala Thr Phe Met Lys Leu Arg Thr Asp Ala Val Leu Pro Leu Thr Val  
                           530                          535                          540  
 Ala Glu Val Gln Lys Leu Leu Gly Pro His Val Glu Gly Leu Lys Ala  
 545                          550                          555                          560  
 Glu Glu Arg His Arg Pro Val Arg Asp Trp Ile Leu Arg Gln Arg Gln  
                           565                          570                          575  
 Asp Asp Leu Asp Thr Leu Gly Leu Gly Leu Gln Gly Gly Ile Pro Asn  
                           580                          585                          590  
 Gly Tyr Leu Val Leu Asp Leu Ser Val Gln Xaa Xaa Leu Ser Gly Thr  
                           595                          600                          605  
 Pro Cys Leu Leu Gly Pro Gly Pro Val Leu Thr Val Leu Ala Leu Leu  
           610                          615                          620  
 Leu Ala Ser Thr Leu Ala  
 625                          630

&lt;210&gt; 211

&lt;211&gt; 1721

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 211

gaattccctg gctgcttgaa tctgttctgc cccctcccca cccatttcac caccaccatg 60  
 acaccgggca cccagtcctc tttcttctcg ctgctgctcc tcacagtgtc tacagttgtt 120  
 acaggttctg gtcattgcaag ctctacccca ggtggagaaa aggagacttc ggctaccag 180  
 agaagttcag tgcccagctc tactgagaag aatgctgtga gtatgaccag cagcgtactc 240

217

```

tccagccaca gccccggttc aggtctctcc accactcagg gacaggatgt cactctggcc 300
ccggccacgg aaccagcttc aggttcagct gccacctggg gacaggatgt cacctcgggc 360
ccagtcacca ggccagccct gggctccacc accccgccag cccacgatgt cacctcagcc 420
ccggacaaca agccagcccc gggctccacc gccccccag cccacgggtgt cacctcggcc 480
ccggacacca ggccgcccc gggctccacc gccccccag cccacgggtgt cacctcggcc 540
ccggacacca ggccgcccc gggctccacc gcgccgcag cccacgggtgt cacctcggcc 600
ccggacacca ggccgcccc gggctccacc gccccccag cccatgggtgt cacctcggcc 660
ccggacaaca ggcccgccctt ggcgtccacc gccctccag tccacaatgt cacctcggcc 720
tcaggctctg catcaggctc agcttctact ctggtgcaca acggcacctc tgccagggtc 780
accacaaccc cagccagcaa gagcactcca ttctcaattc ccagccacca ctctgatact 840
cctaccaccc ttgccagcca tagcaccaag actgatgcc a gtagcactca ccatagcacg 900
gtacctctc tcacctctc caatcacagc acttctcccc agttgtctac tggggtctct 960
ttcttttttc tgtcttttca ctttcaaac ctccagttta attctctctt ggaagatccc 1020
agcaccgact actaccaaga gctgcagaga gacatttctg aaatgttttt gcagatttat 1080
aaacaagggg gttttctggg cctctccaat attaagttca ggccaggatc tgtggtggta 1140
caattgactc tggccttccg agaaggtacc atcaatgtcc acgacgtgga gacacagttc 1200
aatcagtata aaacggaagc agcctctcga tataacctga cgatctcaga cgtcagcgtg 1260
agtgatgtgc catttctctt ctctgccag tctggggctg gggtgccagg ctggggcatc 1320
gcgctgctgg tgcgtgctg tgttctggtt gcgctggcca ttgtctatct cattgccttg 1380
gctgtctgtc agtgccgccc aaagaactac gggcagctgg acatctttcc agcccggtat 1440
acctaccatc ctatgagcga gtacccacc taccacacc atgggcgcta tgtgccctct 1500
agcagtaccg atcgtagccc ctatgagaag gtttctgcag gtaatgggtg cagcagcctc 1560
tcttacacaa acccagcagt ggcagccact tctgccaact tgtaggggca cgtcgcctc 1620
tgagctgagt ggccagccag tgccattcca ctccactcag ggctctctgg gccagtcctc 1680
ctgggagccc ccaccacaac acttcccagg catggaattc c 1721

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&lt;210&gt; 212

&lt;211&gt; 515

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 212

```

Met Thr Pro Gly Thr Gln Ser Pro Phe Phe Leu Leu Leu Leu Thr
1          5          10          15
Val Leu Thr Val Val Thr Gly Ser Gly His Ala Ser Ser Thr Pro Gly
20          25          30
Gly Glu Lys Glu Thr Ser Ala Thr Gln Arg Ser Ser Val Pro Ser Ser
35          40          45
Thr Glu Lys Asn Ala Val Ser Met Thr Ser Ser Val Leu Ser Ser His
50          55          60
Ser Pro Gly Ser Gly Ser Ser Thr Thr Gln Gly Gln Asp Val Thr Leu
65          70          75          80
Ala Pro Ala Thr Glu Pro Ala Ser Gly Ser Ala Ala Thr Trp Gly Gln
85          90          95
Asp Val Thr Ser Val Pro Val Thr Arg Pro Ala Leu Gly Ser Thr Thr
100         105         110
Pro Pro Ala His Asp Val Thr Ser Ala Pro Asp Asn Lys Pro Ala Pro
115         120         125
Gly Ser Thr Ala Pro Pro Ala His Gly Val Thr Ser Ala Pro Asp Thr
130         135         140
Arg Pro Pro Pro Gly Ser Thr Ala Pro Pro Ala His Gly Val Thr Ser
145         150         155         160
Ala Pro Asp Thr Arg Pro Pro Pro Gly Ser Thr Ala Pro Ala Ala His
165         170         175
Gly Val Thr Ser Ala Pro Asp Thr Arg Pro Ala Pro Gly Ser Thr Ala
180         185         190
Pro Pro Ala His Gly Val Thr Ser Ala Pro Asp Asn Arg Pro Ala Leu
195         200         205

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218

Ala Ser Thr Ala Pro Pro Val His Asn Val Thr Ser Ala Ser Gly Ser  
 210 215 220  
 Ala Ser Gly Ser Ala Ser Thr Leu Val His Asn Gly Thr Ser Ala Arg  
 225 230 235 240  
 Ala Thr Thr Thr Pro Ala Ser Lys Ser Thr Pro Phe Ser Ile Pro Ser  
 245 250 255  
 His His Ser Asp Thr Pro Thr Thr Leu Ala Ser His Ser Thr Lys Thr  
 260 265 270  
 Asp Ala Ser Ser Thr His His Ser Thr Val Pro Pro Leu Thr Ser Ser  
 275 280 285  
 Asn His Ser Thr Ser Pro Gln Leu Ser Thr Gly Val Ser Phe Phe Phe  
 290 295 300  
 Leu Ser Phe His Ile Ser Asn Leu Gln Phe Asn Ser Ser Leu Glu Asp  
 305 310 315 320  
 Pro Ser Thr Asp Tyr Tyr Gln Glu Leu Gln Arg Asp Ile Ser Glu Met  
 325 330 335  
 Phe Leu Gln Ile Tyr Lys Gln Gly Gly Phe Leu Gly Leu Ser Asn Ile  
 340 345 350  
 Lys Phe Arg Pro Gly Ser Val Val Gln Leu Thr Leu Ala Phe Arg  
 355 360 365  
 Glu Gly Thr Ile Asn Val His Asp Val Glu Thr Gln Phe Asn Gln Tyr  
 370 375 380  
 Lys Thr Glu Ala Ala Ser Arg Tyr Asn Leu Thr Ile Ser Asp Val Ser  
 385 390 395 400  
 Val Ser Asp Val Pro Phe Pro Phe Ser Ala Gln Ser Gly Ala Gly Val  
 405 410 415  
 Pro Gly Trp Gly Ile Ala Leu Leu Val Leu Val Cys Val Leu Val Ala  
 420 425 430  
 Leu Ala Ile Val Tyr Leu Ile Ala Leu Ala Val Cys Gln Cys Arg Arg  
 435 440 445  
 Lys Asn Tyr Gly Gln Leu Asp Ile Phe Pro Ala Arg Asp Thr Tyr His  
 450 455 460  
 Pro Met Ser Glu Tyr Pro Thr Tyr His Thr His Gly Arg Tyr Val Pro  
 465 470 475 480  
 Pro Ser Ser Thr Asp Arg Ser Pro Tyr Glu Lys Val Ser Ala Gly Asn  
 485 490 495  
 Gly Gly Ser Ser Leu Ser Tyr Thr Asn Pro Ala Val Ala Ala Thr Ser  
 500 505 510  
 Ala Asn Leu  
 515

&lt;210&gt; 213

&lt;211&gt; 5793

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 213

cctggactgg acagagagcg gctatactgg gagctgagcc agctgaccaa cagcatcaca 60  
 gagctggggac cctacaccct ggatagggac agtctctatg tcaatggctt caacccttgg 120  
 agctctgtgc caaccaccag cactcctggg acctccacag tgcacctggc aacctctggg 180  
 actccatcct ccctgcctgg ccacacagcc cctgtccctc tcttgatacc attcaccctc 240  
 aactttacca tcaccaacct gcattatgaa gaaaacatgc aacaccctgg ttccaggaag 300  
 ttcaacacca cggagagggt tctgcagggt ctgctcaagc ccttggttcaa gagcaccagc 360  
 gttggccctc tgtactctgg ctgcagactg accttgctca gacctgagaa acatggggca 420  
 gccactggag tggacgccat ctgcaccctc cgccttgatc ccactggtcc tggactggac 480  
 agagagcggc tatactggga gctgagccag ctgaccaaca gcgttacaga gctgggcccc 540  
 tacaccctgg acagggacag tctctatgtc aatggcttca cccatcggag ctctgtgcc 600

```

accaccagta ttcttgggac ctctgcagtg cacctggaaa cctctgggac tccagcctcc 660
ctccctggcc acacagcccc tggccctctc ctggtgccat tcaccctcaa ctccactatc 720
accaacctgc agtatgagga ggacatgcgt caccctggtt ccaggaagtt caacaccacg 780
gagagagtcc tgcagggtct gctcaagccc ttgttcaaga gcaccagtgt tggccctctg 840
tactctggct gcagactgac cttgctcagg cctgaaaaac gtggggcagc caccggcgtg 900
gacacctctt gcactcaccg ccttgaccct ctaaaccctg gactggacag agagcagcta 960
tactggggagc tgagcaaact gaccctgtgc atcatcgagc tgggccccta cctcctggac 1020
agaggcagtc tctatgtcaa tggtttcacc catcggaact ttgtgcccac caccagcact 1080
cctgggacct ccacagtaca cctaggaacc tctgaaactc catcctccct acctagacct 1140
atagtgcctg gccctctcct ggtgccattc accctcaact tcaccatcac caacttgagc 1200
tatgaggagg ccatgcgaca ccctggctcc aggaagttca ataccacgga gaggttccta 1260
cagggtctgc tcaggccctt gttcaagaat accagtatcg gccctctgta ctccagctgc 1320
agactgacct gctcaggcc agagaaggac aaggcagcca ccagagtga tgccatctgt 1380
accaccacc ctgacctca aagccctgga ctgaacagag agcagctgta ctgggagctg 1440
agccagctga cccacggcat cactgagctg ggcccctaca ccctggacag ggacagtctc 1500
tatgtcgatg gtttactca ttggagcccc ataccaacca ccagcactcc tgggacctcc 1560
atagtgaacc tgggaacctc tgggatccca ccttccctcc ctgaaactac agccaccggc 1620
cctctcctgg tgccattcac actcaacttc accatcata acctacagta tgaggagaac 1680
atgggtcacc ctggctccag gaagttcaac atcacggaga gtgttctgca gggctctgctc 1740
aagcccttgt tcaagagcac cagtgttggc cctctgtatt ctggctgcag actgacctg 1800
ctcaggcctg agaaggacgg agtagccacc agagtggacg ccatctgcac ccaccgccct 1860
gaccccaaaa tccctgggct agacagacag cagctatact gggagctgag ccagctgacc 1920
cacagcatca ctgagctggg accctacacc ctggataggg acagtctcta tgtcaatggt 1980
ttcaccacgc ggagctctgt gccaccacc agcactcctg ggactttcac agtacagccg 2040
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ccattcacc tcaattttac catcattaac ctgcagtatg aggaggacat gcatcgccct 2160
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220

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aaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaa 5793

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&lt;210&gt; 214

&lt;211&gt; 1783

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; VARIANT

&lt;222&gt; (1)...(1783)

&lt;223&gt; Xaa = Any Amino Acid

&lt;400&gt; 214

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Pro Gly Leu Asp Arg Glu Arg Leu Tyr Trp Glu Leu Ser Gln Leu Thr
 1           5           10          15
Asn Ser Ile Thr Glu Leu Gly Pro Tyr Thr Leu Asp Arg Asp Ser Leu
 20          25          30
Tyr Val Asn Gly Phe Asn Pro Trp Ser Ser Val Pro Thr Thr Ser Thr
 35          40          45
Pro Gly Thr Ser Thr Val His Leu Ala Thr Ser Gly Thr Pro Ser Ser
 50          55          60
Leu Pro Gly His Thr Ala Pro Val Pro Leu Leu Ile Pro Phe Thr Leu
 65          70          75          80
Asn Phe Thr Ile Thr Asn Leu His Tyr Glu Glu Asn Met Gln His Pro
 85          90          95
Gly Ser Arg Lys Phe Asn Thr Thr Glu Arg Val Leu Gln Gly Leu Leu
100         105         110
Lys Pro Leu Phe Lys Ser Thr Ser Val Gly Pro Leu Tyr Ser Gly Cys
115         120         125
Arg Leu Thr Leu Leu Arg Pro Glu Lys His Gly Ala Ala Thr Gly Val

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221

130	135	140
Asp Ala Ile Cys Thr	Leu Arg Leu Asp Pro Thr Gly Pro Gly Leu Asp	
145	150	155
Arg Glu Arg Leu Tyr Trp Glu Leu Ser Gln Leu Thr Asn Ser Val Thr		160
	165	170
Glu Leu Gly Pro Tyr Thr Leu Asp Arg Asp Ser Leu Tyr Val Asn Gly		175
	180	185
Phe Thr His Arg Ser Ser Val Pro Thr Thr Ser Ile Pro Gly Thr Ser		190
	195	200
Ala Val His Leu Glu Thr Ser Gly Thr Pro Ala Ser Leu Pro Gly His		205
	210	215
Thr Ala Pro Gly Pro Leu Leu Val Pro Phe Thr Leu Asn Phe Thr Ile		220
225	230	235
Thr Asn Leu Gln Tyr Glu Glu Asp Met Arg His Pro Gly Ser Arg Lys		240
	245	250
Phe Asn Thr Thr Glu Arg Val Leu Gln Gly Leu Leu Lys Pro Leu Phe		255
	260	265
Lys Ser Thr Ser Val Gly Pro Leu Tyr Ser Gly Cys Arg Leu Thr Leu		270
	275	280
Leu Arg Pro Glu Lys Arg Gly Ala Ala Thr Gly Val Asp Thr Ile Cys		285
	290	295
Thr His Arg Leu Asp Pro Leu Asn Pro Gly Leu Asp Arg Glu Gln Leu		300
305	310	315
Tyr Trp Glu Leu Ser Lys Leu Thr Arg Gly Ile Ile Glu Leu Gly Pro		320
	325	330
Tyr Leu Leu Asp Arg Gly Ser Leu Tyr Val Asn Gly Phe Thr His Arg		335
	340	345
Asn Phe Val Pro Ile Thr Ser Thr Pro Gly Thr Ser Thr Val His Leu		350
	355	360
Gly Thr Ser Glu Thr Pro Ser Ser Leu Pro Arg Pro Ile Val Pro Gly		365
	370	375
Pro Leu Leu Val Pro Phe Thr Leu Asn Phe Thr Ile Thr Asn Leu Gln		380
385	390	395
Tyr Glu Glu Ala Met Arg His Pro Gly Ser Arg Lys Phe Asn Thr Thr		400
	405	410
Glu Arg Val Leu Gln Gly Leu Leu Arg Pro Leu Phe Lys Asn Thr Ser		415
	420	425
Ile Gly Pro Leu Tyr Ser Ser Cys Arg Leu Thr Leu Leu Arg Pro Glu		430
	435	440
Lys Asp Lys Ala Ala Thr Arg Val Asp Ala Ile Cys Thr His His Pro		445
	450	455
Asp Pro Gln Ser Pro Gly Leu Asn Arg Glu Gln Leu Tyr Trp Glu Leu		460
465	470	475
Ser Gln Leu Thr His Gly Ile Thr Glu Leu Gly Pro Tyr Thr Leu Asp		480
	485	490
Arg Asp Ser Leu Tyr Val Asp Gly Phe Thr His Trp Ser Pro Ile Pro		495
	500	505
Thr Thr Ser Thr Pro Gly Thr Ser Ile Val Asn Leu Gly Thr Ser Gly		510
	515	520
Ile Pro Pro Ser Leu Pro Glu Thr Thr Ala Thr Gly Pro Leu Leu Val		525
	530	535
Pro Phe Thr Leu Asn Phe Thr Ile Thr Asn Leu Gln Tyr Glu Glu Asn		540
545	550	555
Met Gly His Pro Gly Ser Arg Lys Phe Asn Ile Thr Glu Ser Val Leu		560
	565	570
Gln Gly Leu Leu Lys Pro Leu Phe Lys Ser Thr Ser Val Gly Pro Leu		575
	580	585
Tyr Ser Gly Cys Arg Leu Thr Leu Leu Arg Pro Glu Lys Asp Gly Val		590

595	600	605
Ala Thr Arg Val Asp	Ala Ile Cys Thr His Arg	Pro Asp Pro Lys Ile
610	615	620
Pro Gly Leu Asp Arg	Gln Gln Leu Tyr Trp	Glu Leu Ser Gln Leu Thr
625	630	635
His Ser Ile Thr	Glu Leu Gly Pro Tyr Thr	Leu Asp Arg Asp Ser Leu
	645	650
		655
Tyr Val Asn Gly Phe Thr Gln Arg Ser Ser Val Pro Thr Thr Ser Thr		
	660	665
		670
Pro Gly Thr Phe Thr Val Gln Pro Glu Thr Ser Glu Thr Pro Ser Ser		
	675	680
		685
Leu Pro Gly Pro Thr Ala Thr Gly Pro Val Leu Leu Pro Phe Thr Leu		
	690	695
		700
Asn Phe Thr Ile Ile Asn Leu Gln Tyr Glu Glu Asp Met His Arg Pro		
705	710	715
Gly Ser Arg Lys Phe Asn Thr Thr Glu Arg Val Leu Gln Gly Leu Leu		
	725	730
		735
Met Pro Leu Phe Lys Asn Thr Ser Val Ser Ser Leu Tyr Ser Gly Cys		
	740	745
		750
Arg Leu Thr Leu Leu Arg Pro Glu Lys Asp Gly Ala Ala Thr Arg Val		
	755	760
		765
Asp Ala Val Cys Thr His Arg Pro Asp Pro Lys Ser Pro Gly Leu Asp		
	770	775
		780
Arg Glu Arg Leu Tyr Trp Lys Leu Ser Gln Leu Thr His Gly Ile Thr		
785	790	795
Glu Leu Gly Pro Tyr Thr Leu Asp Arg His Ser Leu Tyr Val Asn Gly		
	805	810
		815
Phe Thr His Gln Ser Ser Met Thr Thr Thr Arg Thr Pro Asp Thr Ser		
	820	825
		830
Thr Met His Leu Ala Thr Ser Arg Thr Pro Ala Ser Leu Ser Gly Pro		
	835	840
		845
Thr Thr Ala Ser Pro Leu Leu Val Leu Phe Thr Ile Asn Phe Thr Ile		
	850	855
		860
Thr Asn Leu Arg Tyr Glu Glu Asn Met His His Pro Gly Ser Arg Lys		
865	870	875
Phe Asn Thr Thr Glu Arg Val Leu Gln Gly Leu Leu Arg Pro Val Phe		
	885	890
		895
Lys Asn Thr Ser Val Gly Pro Leu Tyr Ser Gly Cys Arg Leu Thr Leu		
	900	905
		910
Leu Arg Pro Lys Lys Asp Gly Ala Ala Thr Lys Val Asp Ala Ile Cys		
	915	920
		925
Thr Tyr Arg Pro Asp Pro Lys Ser Pro Gly Leu Asp Arg Glu Gln Leu		
	930	935
		940
Tyr Trp Glu Leu Ser Gln Leu Thr His Ser Ile Thr Glu Leu Gly Pro		
945	950	955
Tyr Thr Leu Asp Arg Asp Ser Leu Tyr Val Asn Gly Phe Thr Gln Arg		
	965	970
		975
Ser Ser Val Pro Thr Thr Ser Ile Pro Gly Thr Pro Thr Val Asp Leu		
	980	985
		990
Gly Thr Ser Gly Thr Pro Val Ser Lys Pro Gly Pro Ser Ala Ala Ser		
	995	1000
		1005
Pro Leu Leu Val Leu Phe Thr Leu Asn Phe Thr Ile Thr Asn Leu Arg		
	1010	1015
		1020
Tyr Glu Glu Asn Met Gln His Pro Gly Ser Arg Lys Phe Asn Thr Thr		
1025	1030	1035
Glu Arg Val Leu Gln Gly Leu Leu Arg Ser Leu Phe Lys Ser Thr Ser		
	1045	1050
		1055
Val Gly Pro Leu Tyr Ser Gly Cys Arg Leu Thr Leu Leu Arg Pro Glu		

1060				1065				1070							
Lys	Asp	Gly	Thr	Ala	Thr	Gly	Val	Asp	Ala	Ile	Cys	Thr	His	His	Pro
1075				1080				1085							
Asp	Pro	Lys	Ser	Pro	Arg	Leu	Asp	Arg	Glu	Gln	Leu	Tyr	Trp	Glu	Leu
1090				1095				1100							
Ser	Gln	Leu	Thr	His	Asn	Ile	Thr	Glu	Leu	Gly	His	Tyr	Ala	Leu	Asp
1105				1110				1115				1120			
Asn	Asp	Ser	Leu	Phe	Val	Asn	Gly	Phe	Thr	His	Arg	Ser	Ser	Val	Ser
1125				1130				1135							
Thr	Thr	Ser	Thr	Pro	Gly	Thr	Pro	Thr	Val	Tyr	Leu	Gly	Ala	Ser	Lys
1140				1145				1150							
Thr	Pro	Ala	Ser	Ile	Phe	Gly	Pro	Ser	Ala	Ala	Ser	His	Leu	Leu	Ile
1155				1160				1165							
Leu	Phe	Thr	Leu	Asn	Phe	Thr	Ile	Thr	Asn	Leu	Arg	Tyr	Glu	Glu	Asn
1170				1175				1180							
Met	Trp	Pro	Gly	Ser	Arg	Lys	Phe	Asn	Thr	Thr	Glu	Arg	Val	Leu	Gln
1185				1190				1195				1200			
Gly	Leu	Leu	Arg	Pro	Leu	Phe	Lys	Asn	Thr	Ser	Val	Gly	Pro	Leu	Tyr
1205				1210				1215							
Ser	Gly	Ser	Arg	Leu	Thr	Leu	Leu	Arg	Pro	Glu	Lys	Asp	Gly	Glu	Ala
1220				1225				1230							
Thr	Gly	Val	Asp	Ala	Ile	Cys	Thr	His	Arg	Pro	Asp	Pro	Thr	Gly	Pro
1235				1240				1245							
Gly	Leu	Asp	Arg	Glu	Gln	Leu	Tyr	Leu	Glu	Leu	Ser	Gln	Leu	Thr	His
1250				1255				1260							
Ser	Ile	Thr	Glu	Leu	Gly	Pro	Tyr	Thr	Leu	Asp	Arg	Asp	Ser	Leu	Tyr
1265				1270				1275				1280			
Val	Asn	Gly	Phe	Thr	His	Arg	Ser	Ser	Val	Pro	Thr	Thr	Ser	Thr	Gly
1285				1290				1295							
Val	Val	Ser	Glu	Glu	Pro	Phe	Thr	Leu	Asn	Phe	Thr	Ile	Asn	Asn	Leu
1300				1305				1310							
Arg	Tyr	Met	Ala	Asp	Met	Gly	Gln	Pro	Gly	Ser	Leu	Lys	Phe	Asn	Ile
1315				1320				1325							
Thr	Asp	Asn	Val	Met	Lys	His	Leu	Leu	Ser	Pro	Leu	Phe	Gln	Arg	Ser
1330				1335				1340							
Ser	Leu	Gly	Ala	Arg	Tyr	Thr	Gly	Cys	Arg	Val	Ile	Ala	Leu	Arg	Ser
1345				1350				1355				1360			
Val	Lys	Asn	Gly	Ala	Glu	Thr	Arg	Val	Asp	Leu	Leu	Cys	Thr	Tyr	Leu
1365				1370				1375							
Gln	Pro	Leu	Ser	Gly	Pro	Gly	Leu	Pro	Ile	Lys	Gln	Val	Phe	His	Glu
1380				1385				1390							
Leu	Ser	Gln	Gln	Thr	His	Gly	Ile	Thr	Arg	Leu	Gly	Pro	Tyr	Ser	Leu
1395				1400				1405							
Asp	Lys	Asp	Ser	Leu	Tyr	Leu	Asn	Gly	Tyr	Asn	Glu	Pro	Gly	Leu	Asp
1410				1415				1420							
Glu	Pro	Pro	Thr	Thr	Pro	Lys	Pro	Ala	Thr	Thr	Phe	Leu	Pro	Pro	Leu
1425				1430				1435				1440			
Ser	Glu	Ala	Thr	Thr	Ala	Met	Gly	Tyr	His	Leu	Lys	Thr	Leu	Thr	Leu
1445				1450				1455							
Asn	Phe	Thr	Ile	Ser	Asn	Leu	Gln	Tyr	Ser	Pro	Asp	Met	Gly	Lys	Gly
1460				1465				1470							
Ser	Ala	Thr	Phe	Asn	Ser	Thr	Glu	Gly	Val	Leu	Gln	His	Leu	Leu	Arg
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Pro	Leu	Phe	Gln	Lys	Ser	Ser	Met	Gly	Pro	Phe	Tyr	Leu	Gly	Cys	Gln
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Leu	Ile	Ser	Leu	Arg	Pro	Glu	Lys	Asp	Gly	Ala	Ala	Thr	Gly	Val	Asp
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Thr	Thr	Cys	Thr	Tyr	His	Pro	Asp	Pro	Val	Gly	Pro	Gly	Leu	Asp	Ile

224

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Leu	Gly	Phe	Tyr	Val	Leu	Asp	Arg	Asp	Ser	Leu	Phe	Ile	Asn	Gly	Tyr					
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Ala	Pro	Gln	Asn	Leu	Ser	Ile	Arg	Gly	Glu	Tyr	Gln	Ile	Asn	Phe	His					
										1570			1575				1580			
Ile	Val	Asn	Trp	Asn	Leu	Ser	Asn	Pro	Asp	Pro	Thr	Ser	Ser	Glu	Tyr					
										1585			1590				1595			
Ile	Thr	Leu	Leu	Arg	Asp	Ile	Gln	Asp	Lys	Val	Thr	Thr	Leu	Tyr	Lys					
										1605			1610				1615			
Gly	Ser	Gln	Leu	His	Asp	Thr	Phe	Arg	Phe	Cys	Leu	Val	Thr	Asn	Leu					
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Thr	Met	Asp	Ser	Val	Leu	Val	Thr	Val	Lys	Ala	Leu	Phe	Ser	Ser	Asn					
										1635			1640				1645			
Leu	Asp	Pro	Ser	Leu	Val	Glu	Gln	Val	Phe	Leu	Asp	Lys	Thr	Leu	Asn					
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Ala	Ser	Phe	His	Trp	Leu	Gly	Ser	Thr	Tyr	Gln	Leu	Val	Asp	Ile	His					
										1665			1670				1675			
Val	Thr	Glu	Met	Glu	Ser	Ser	Val	Tyr	Gln	Pro	Thr	Ser	Ser	Ser	Ser					
										1685			1690				1695			
Thr	Gln	His	Phe	Tyr	Xaa	Asn	Phe	Thr	Ile	Thr	Asn	Leu	Pro	Tyr	Ser					
										1700			1705				1710			
Gln	Asp	Lys	Ala	Gln	Pro	Gly	Thr	Thr	Asn	Tyr	Gln	Arg	Asn	Lys	Arg					
										1715			1720				1725			
Asn	Ile	Glu	Asp	Ala	Val	Arg	Arg	Gly	Cys	Ser	Thr	Asn	Ser	Ser	Glu					
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Thr	Ala	Ala	Ser	Arg	Val	Ile	Phe	Leu	Thr	Val	Lys	Phe	Gln	His	Ser					
										1745			1750				1755			
Gly	Leu	Ser	Pro	Thr	Gly	Thr	Thr	Pro	Gly	Trp	Thr	Pro	Cys	Val	Thr					
										1765			1770				1775			
Ser	Arg	His	Trp	Leu	Gly	Glu														
										1780										

&lt;210&gt; 215

&lt;211&gt; 5797

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 215

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&lt;210&gt; 216

&lt;211&gt; 1148

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 216

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Arg Leu Thr Leu Leu Arg Pro Glu Lys Asp Gly Ala Ala Thr Arg Val
20      25      30
Asp Ala Val Cys Thr His Arg Pro Asp Pro Lys Ser Pro Gly Leu Asp
35      40      45
Arg Glu Arg Leu Tyr Trp Lys Leu Ser Gln Leu Thr His Gly Ile Thr
50      55      60
Glu Leu Gly Pro Tyr Thr Leu Asp Arg His Ser Leu Tyr Val Asn Gly
65      70      75      80
Phe Thr His Gln Ser Ser Met Thr Thr Thr Arg Thr Pro Asp Thr Ser
85      90      95
Thr Met His Leu Ala Thr Ser Arg Thr Pro Ala Ser Leu Ser Gly Pro
100     105     110
Thr Thr Ala Ser Pro Leu Leu Val Leu Phe Thr Ile Asn Phe Thr Ile
115     120     125
Thr Asn Leu Arg Tyr Glu Glu Asn Met His His Pro Gly Ser Arg Lys
130     135     140
Phe Asn Thr Thr Glu Arg Val Leu Gln Gly Leu Leu Arg Pro Val Phe
145     150     155     160
Lys Asn Thr Ser Val Gly Pro Leu Tyr Ser Gly Cys Arg Leu Thr Leu
165     170     175
Leu Arg Pro Lys Lys Asp Gly Ala Ala Thr Lys Val Asp Ala Ile Cys
180     185     190
Thr Tyr Arg Pro Asp Pro Lys Ser Pro Gly Leu Asp Arg Glu Gln Leu
195     200     205
Tyr Trp Glu Leu Ser Gln Leu Thr His Ser Ile Thr Glu Leu Gly Pro
210     215     220
Tyr Thr Leu Asp Arg Asp Ser Leu Tyr Val Asn Gly Phe Thr Gln Arg

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225						230						235						240
Ser	Ser	Val	Pro	Thr	Thr	Ser	Ile	Pro	Gly	Thr	Pro	Thr	Val	Asp	Leu			
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Gly	Thr	Ser	Gly	Thr	Pro	Val	Ser	Lys	Pro	Gly	Pro	Ser	Ala	Ala	Ser			
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Pro	Leu	Leu	Val	Leu	Phe	Thr	Leu	Asn	Phe	Thr	Ile	Thr	Asn	Leu	Arg			
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Tyr	Glu	Glu	Asn	Met	Gln	His	Pro	Gly	Ser	Arg	Lys	Phe	Asn	Thr	Thr			
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Glu	Arg	Val	Leu	Gln	Gly	Leu	Leu	Arg	Ser	Leu	Phe	Lys	Ser	Thr	Ser			
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Val	Gly	Pro	Leu	Tyr	Ser	Gly	Cys	Arg	Leu	Thr	Leu	Leu	Arg	Pro	Glu			
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Lys	Asp	Gly	Thr	Ala	Thr	Gly	Val	Asp	Ala	Ile	Cys	Thr	His	His	Pro			
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Asp	Pro	Lys	Ser	Pro	Arg	Leu	Asp	Arg	Glu	Gln	Leu	Tyr	Trp	Glu	Leu			
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Ser	Gln	Leu	Thr	His	Asn	Ile	Thr	Glu	Leu	Gly	His	Tyr	Ala	Leu	Asp			
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Asn	Asp	Ser	Leu	Phe	Val	Asn	Gly	Phe	Thr	His	Arg	Ser	Ser	Val	Ser			
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Thr	Thr	Ser	Thr	Pro	Gly	Thr	Pro	Thr	Val	Tyr	Leu	Gly	Ala	Ser	Lys			
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Thr	Pro	Ala	Ser	Ile	Phe	Gly	Pro	Ser	Ala	Ala	Ser	His	Leu	Leu	Ile			
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Leu	Phe	Thr	Leu	Asn	Phe	Thr	Ile	Thr	Asn	Leu	Arg	Tyr	Glu	Glu	Asn			
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Met	Trp	Pro	Gly	Ser	Arg	Lys	Phe	Asn	Thr	Thr	Glu	Arg	Val	Leu	Gln			
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Gly	Leu	Leu	Arg	Pro	Leu	Phe	Lys	Asn	Thr	Ser	Val	Gly	Pro	Leu	Tyr			
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Ser	Gly	Ser	Arg	Leu	Thr	Leu	Leu	Arg	Pro	Glu	Lys	Asp	Gly	Glu	Ala			
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Thr	Gly	Val	Asp	Ala	Ile	Cys	Thr	His	Arg	Pro	Asp	Pro	Thr	Gly	Pro			
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Gly	Leu	Asp	Arg	Glu	Gln	Leu	Tyr	Leu	Glu	Leu	Ser	Gln	Leu	Thr	His			
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Ser	Ile	Thr	Glu	Leu	Gly	Pro	Tyr	Thr	Leu	Asp	Arg	Asp	Ser	Leu	Tyr			
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Val	Asn	Gly	Phe	Thr	His	Arg	Ser	Ser	Val	Pro	Thr	Thr	Ser	Thr	Gly			
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Val	Val	Ser	Glu	Glu	Pro	Phe	Thr	Leu	Asn	Phe	Thr	Ile	Asn	Asn	Leu			
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Arg	Tyr	Met	Ala	Asp	Met	Gly	Gln	Pro	Gly	Ser	Leu	Lys	Phe	Asn	Ile			
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Thr	Asp	Asn	Val	Met	Lys	His	Leu	Leu	Ser	Pro	Leu	Phe	Gln	Arg	Ser			
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Ser	Leu	Gly	Ala	Arg	Tyr	Thr	Gly	Cys	Arg	Val	Ile	Ala	Leu	Arg	Ser			
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Val	Lys	Asn	Gly	Ala	Glu	Thr	Arg	Val	Asp	Leu	Leu	Cys	Thr	Tyr	Leu			
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Gln	Pro	Leu	Ser	Gly	Pro	Gly	Leu	Pro	Ile	Lys	Gln	Val	Phe	His	Glu			
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Leu	Ser	Gln	Gln	Thr	His	Gly	Ile	Thr</										

690	695	700
Ser Glu Ala Thr Thr	Ala Met Gly Tyr His	Leu Lys Thr Leu Thr Leu
705	710	715
Asn Phe Thr Ile Ser	Asn Leu Gln Tyr Ser	Pro Asp Met Gly Lys Gly
725	730	735
Ser Ala Thr Phe Asn	Ser Thr Glu Gly Val	Leu Gln His Leu Leu Arg
740	745	750
Pro Leu Phe Gln Lys	Ser Ser Met Gly Pro	Phe Tyr Leu Gly Cys Gln
755	760	765
Leu Ile Ser Leu Arg	Pro Glu Lys Asp Gly	Ala Ala Thr Gly Val Asp
770	775	780
Thr Thr Cys Thr Tyr	His Pro Asp Pro Val	Gly Pro Gly Leu Asp Ile
785	790	795
Gln Gln Leu Tyr Trp	Glu Leu Ser Gln Leu	Thr His Gly Val Thr Gln
805	810	815
Leu Gly Phe Tyr Val	Leu Asp Arg Asp Ser	Leu Phe Ile Asn Gly Tyr
820	825	830
Ala Pro Gln Asn Leu	Ser Ile Arg Gly Glu	Tyr Gln Ile Asn Phe His
835	840	845
Ile Val Asn Trp Asn	Leu Ser Asn Pro Asp	Pro Thr Ser Ser Glu Tyr
850	855	860
Ile Thr Leu Leu Arg	Asp Ile Gln Asp Lys	Val Thr Thr Leu Tyr Lys
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Gly Ser Gln Leu His	Asp Thr Phe Arg Phe	Cys Leu Val Thr Asn Leu
885	890	895
Thr Met Asp Ser Val	Leu Val Thr Val Lys	Ala Leu Phe Ser Ser Asn
900	905	910
Leu Asp Pro Ser Leu	Val Glu Gln Val Phe	Leu Asp Lys Thr Leu Asn
915	920	925
Ala Ser Phe His Trp	Leu Gly Ser Thr Tyr	Gln Leu Val Asp Ile His
930	935	940
Val Thr Glu Met Glu	Ser Ser Val Tyr Gln	Pro Thr Ser Ser Ser Ser
945	950	955
Thr Gln His Phe Tyr	Pro Asn Phe Thr Ile	Thr Asn Leu Pro Tyr Ser
965	970	975
Gln Asp Lys Ala Gln	Pro Gly Thr Thr Asn	Tyr Gln Arg Asn Lys Arg
980	985	990
Asn Ile Glu Asp Ala	Leu Asn Gln Leu Phe	Arg Asn Ser Ser Ile Lys
995	1000	1005
Ser Tyr Phe Ser Asp	Cys Gln Val Ser Thr	Phe Arg Ser Val Pro Asn
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Arg His His Thr Gly	Val Asp Ser Leu Cys	Asn Phe Ser Pro Leu Ala
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Arg Arg Val Asp Arg	Val Ala Ile Tyr Glu	Glu Phe Leu Arg Met Thr
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Arg Asn Gly Thr Gln	Leu Gln Asn Phe Thr	Leu Asp Arg Ser Ser Val
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Leu Val Asp Gly Tyr	Ser Pro Asn Arg Asn	Glu Pro Leu Thr Gly Asn
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Ser Asp Leu Pro Phe	Trp Ala Val Ile Phe	Ile Gly Leu Ala Gly Leu
1090	1095	1100
Leu Gly Leu Ile Thr	Cys Leu Ile Cys Gly	Val Leu Val Thr Thr Arg
1105	1110	1115
Arg Arg Lys Lys Glu	Gly Glu Tyr Asn Val	Gln Gln Cys Pro Gly
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Tyr Tyr Gln Ser His	Leu Asp Leu Glu Asp	Leu Gln
1140	1145	

229

<210> 217  
 <211> 1890  
 <212> PRT  
 <213> Homo sapiens

<400> 217

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      20           25           30
Leu Asp Arg Asp Ser Leu Tyr Val Asn Gly Phe Asn Pro Trp Ser Ser
      35           40           45
Val Pro Thr Thr Ser Thr Pro Gly Thr Ser Thr Val His Leu Ala Thr
      50           55           60
Ser Gly Thr Pro Ser Ser Leu Pro Gly His Thr Ala Pro Val Pro Leu
      65           70           75           80
Leu Ile Pro Phe Thr Leu Asn Phe Thr Ile Thr Asn Leu His Tyr Glu
      85           90           95
Glu Asn Met Gln His Pro Gly Ser Arg Lys Phe Asn Thr Thr Glu Arg
      100          105          110
Val Leu Gln Gly Leu Leu Lys Pro Leu Phe Lys Ser Thr Ser Val Gly
      115          120          125
Pro Leu Tyr Ser Gly Cys Arg Leu Thr Leu Leu Arg Pro Glu Lys His
      130          135          140
Gly Ala Ala Thr Gly Val Asp Ala Ile Cys Thr Leu Arg Leu Asp Pro
      145          150          155          160
Thr Gly Pro Gly Leu Asp Arg Glu Arg Leu Tyr Trp Glu Leu Ser Gln
      165          170          175
Leu Thr Asn Ser Val Thr Glu Leu Gly Pro Tyr Thr Leu Asp Arg Asp
      180          185          190
Ser Leu Tyr Val Asn Gly Phe Thr His Arg Ser Ser Val Pro Thr Thr
      195          200          205
Ser Ile Pro Gly Thr Ser Ala Val His Leu Glu Thr Ser Gly Thr Pro
      210          215          220
Ala Ser Leu Pro Gly His Thr Ala Pro Gly Pro Leu Leu Val Pro Phe
      225          230          235          240
Thr Leu Asn Phe Thr Ile Thr Asn Leu Gln Tyr Glu Glu Asp Met Arg
      245          250          255
His Pro Gly Ser Arg Lys Phe Asn Thr Thr Glu Arg Val Leu Gln Gly
      260          265          270
Leu Leu Lys Pro Leu Phe Lys Ser Thr Ser Val Gly Pro Leu Tyr Ser
      275          280          285
Gly Cys Arg Leu Thr Leu Leu Arg Pro Glu Lys Arg Gly Ala Ala Thr
      290          295          300
Gly Val Asp Thr Ile Cys Thr His Arg Leu Asp Pro Leu Asn Pro Gly
      305          310          315          320
Leu Asp Arg Glu Gln Leu Tyr Trp Glu Leu Ser Lys Leu Thr Arg Gly
      325          330          335
Ile Ile Glu Leu Gly Pro Tyr Leu Leu Asp Arg Gly Ser Leu Tyr Val
      340          345          350
Asn Gly Phe Thr His Arg Asn Phe Val Pro Ile Thr Ser Thr Pro Gly
      355          360          365
Thr Ser Thr Val His Leu Gly Thr Ser Glu Thr Pro Ser Ser Leu Pro
      370          375          380
Arg Pro Ile Val Pro Gly Pro Leu Leu Val Pro Phe Thr Leu Asn Phe
      385          390          395          400
Thr Ile Thr Asn Leu Gln Tyr Glu Glu Ala Met Arg His Pro Gly Ser

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865		870		875		880
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Leu Leu Arg Pro Val	Phe Lys Asn Thr Ser Val Gly Pro Leu Tyr Ser					
	900	905			910	
Gly Cys Arg Leu Thr	Leu Leu Arg Pro Lys Lys Asp Gly Ala Ala Thr					
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Lys Val Asp Ala Ile	Cys Thr Tyr Arg Pro Asp Pro Lys Ser Pro Gly					
	930	935			940	
Leu Asp Arg Glu Gln	Leu Tyr Trp Glu Leu Ser Gln Leu Thr His Ser					
945	950	955			960	
Ile Thr Glu Leu Gly	Pro Tyr Thr Leu Asp Arg Asp Ser Leu Tyr Val					
	965	970			975	
Asn Gly Phe Thr Gln	Arg Ser Ser Val Pro Thr Thr Ser Ile Pro Gly					
	980	985			990	
Thr Pro Thr Val Asp	Leu Gly Thr Ser Gly Thr Pro Val Ser Lys Pro					
	995	1000			1005	
Gly Pro Ser Ala Ala	Ser Pro Leu Leu Val Leu Phe Thr Leu Asn Phe					
	1010	1015			1020	
Thr Ile Thr Asn Leu	Arg Tyr Glu Glu Asn Met Gln His Pro Gly Ser					
1025	1030	1035			1040	
Arg Lys Phe Asn Thr	Thr Glu Arg Val Leu Gln Gly Leu Leu Arg Ser					
	1045	1050			1055	
Leu Phe Lys Ser Thr	Ser Val Gly Pro Leu Tyr Ser Gly Cys Arg Leu					
	1060	1065			1070	
Thr Leu Leu Arg Pro	Glu Lys Asp Gly Thr Ala Thr Gly Val Asp Ala					
	1075	1080			1085	
Ile Cys Thr His His	Pro Asp Pro Lys Ser Pro Arg Leu Asp Arg Glu					
	1090	1095			1100	
Gln Leu Tyr Trp Glu	Leu Ser Gln Leu Thr His Asn Ile Thr Glu Leu					
1105	1110	1115			1120	
Gly Pro Tyr Ala Leu	Asp Asn Asp Ser Leu Phe Val Asn Gly Phe Thr					
	1125	1130			1135	
His Arg Ser Ser Val	Ser Thr Thr Ser Thr Pro Gly Thr Pro Thr Val					
	1140	1145			1150	
Tyr Leu Gly Ala Ser	Lys Thr Pro Ala Ser Ile Phe Gly Pro Ser Ala					
	1155	1160			1165	
Ala Ser His Leu Leu	Ile Leu Phe Thr Leu Asn Phe Thr Ile Thr Asn					
	1170	1175			1180	
Leu Arg Tyr Glu Glu	Asn Met Trp Pro Gly Ser Arg Lys Phe Asn Thr					
1185	1190	1195			1200	
Thr Glu Arg Val Leu	Gln Gly Leu Leu Arg Pro Leu Phe Lys Asn Thr					
	1205	1210			1215	
Ser Val Gly Pro Leu	Tyr Ser Gly Cys Arg Leu Thr Leu Leu Arg Pro					
	1220	1225			1230	
Glu Lys Asp Gly Glu	Ala Thr Gly Val Asp Ala Ile Cys Thr His Arg					
	1235	1240			1245	
Pro Asp Pro Thr Gly	Pro Gly Leu Asp Arg Glu Gln Leu Tyr Leu Glu					
	1250	1255			1260	
Leu Ser Gln Leu Thr	His Ser Ile Thr Glu Leu Gly Pro Tyr Thr Leu					
1265	1270	1275			1280	
Asp Arg Asp Ser Leu	Tyr Val Asn Gly Phe Thr His Arg Ser Ser Val					
	1285	1290			1295	
Pro Thr Thr Ser Thr	Gly Val Val Ser Glu Glu Pro Phe Thr Leu Asn					
	1300	1305			1310	
Phe Thr Ile Asn Asn	Leu Arg Tyr Met Ala Asp Met Gly Gln Pro Gly					
	1315	1320			1325	
Ser Leu Lys Phe Asn	Ile Thr Asp Asn Val Met Gln His Leu Leu Ser					

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1330	1335	1340
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Val Ile Ala Leu Arg Ser Val Lys Asn Gly Ala Glu Thr Arg Val Asp		1360
	1365	1370
Leu Leu Cys Thr Tyr Leu Gln Pro Leu Ser Gly Pro Gly Leu Pro Ile		1375
	1380	1385
Lys Gln Val Phe His Glu Leu Ser Gln Gln Thr His Gly Ile Thr Arg		1390
	1395	1400
Leu Gly Pro Tyr Ser Leu Asp Lys Asp Ser Leu Tyr Leu Asn Gly Tyr		1405
	1410	1415
Asn Glu Pro Gly Pro Asp Glu Pro Pro Thr Thr Pro Lys Pro Ala Thr		1420
1425	1430	1435
Thr Phe Leu Pro Pro Leu Ser Glu Ala Thr Thr Ala Met Gly Tyr His		1440
	1445	1450
Leu Lys Thr Leu Thr Leu Asn Phe Thr Ile Ser Asn Leu Gln Tyr Ser		1455
	1460	1465
Pro Asp Met Gly Lys Gly Ser Ala Thr Phe Asn Ser Thr Glu Gly Val		1470
	1475	1480
Leu Gln His Leu Leu Arg Pro Leu Phe Gln Lys Ser Ser Met Gly Pro		1485
	1490	1495
Phe Tyr Leu Gly Cys Gln Leu Ile Ser Leu Arg Pro Glu Lys Asp Gly		1500
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Ala Ala Thr Gly Val Asp Thr Thr Cys Thr Tyr His Pro Asp Pro Val		1520
	1525	1530
Gly Pro Gly Leu Asp Ile Gln Gln Leu Tyr Trp Glu Leu Ser Gln Leu		1535
	1540	1545
Thr His Gly Val Thr Gln Leu Gly Phe Tyr Val Leu Asp Arg Asp Ser		1550
	1555	1560
Leu Phe Ile Asn Gly Tyr Ala Pro Gln Asn Leu Ser Ile Arg Gly Glu		1565
	1570	1575
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Arg Asn Ser Ser Ile Lys Ser Tyr Phe Ser Asp Cys Gln Val Ser Thr		1740
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Phe Arg Ser Val Pro Asn Arg His His Thr Gly Val Asp Ser Leu Cys		1760
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Asn Phe Ser Pro Leu Ala Arg Arg Val Asp Arg Val Ala Ile Tyr Glu		1775
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234

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239

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agccaccacc aggcctgatt gtaattttt ttttttttt tactgggtat gggaaggag 4080
aaataaaatc atcaaacccc aaaaaaaaa aaaaaaaaa aaaaaaaaa aaaaa 4135

```

&lt;210&gt; 221

&lt;211&gt; 689

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 221

```

Met Ala Pro Trp Pro Glu Leu Gly Asp Ala Gln Pro Asn Pro Asp Lys
1          5          10          15
Tyr Leu Glu Gly Ala Ala Gly Gln Gln Pro Thr Ala Pro Asp Lys Ser
20          25          30
Lys Glu Thr Asn Lys Asn Asn Thr Glu Ala Pro Val Thr Lys Ile Glu
35          40          45
Leu Leu Pro Ser Tyr Ser Thr Ala Thr Leu Ile Asp Glu Pro Thr Glu
50          55          60
Val Asp Asp Pro Trp Asn Leu Pro Thr Leu Gln Asp Ser Gly Ile Lys
65          70          75          80
Trp Ser Glu Arg Asp Thr Lys Gly Lys Ile Leu Cys Phe Phe Gln Gly
85          90          95
Ile Gly Arg Leu Ile Leu Leu Leu Gly Phe Leu Tyr Phe Phe Val Cys
100          105          110
Ser Leu Asp Ile Leu Ser Ser Ala Phe Gln Leu Val Gly Gly Lys Met
115          120          125
Ala Gly Gln Phe Phe Ser Asn Ser Ser Ile Met Ser Asn Pro Leu Leu
130          135          140
Gly Leu Val Ile Gly Val Leu Val Thr Val Leu Val Gln Ser Ser Ser
145          150          155          160
Thr Ser Thr Ser Ile Val Val Ser Met Val Ser Ser Ser Leu Leu Thr
165          170          175
Val Arg Ala Ala Ile Pro Ile Ile Met Gly Ala Asn Ile Gly Thr Ser
180          185          190
Ile Thr Asn Thr Ile Val Ala Leu Met Gln Val Gly Asp Arg Ser Glu
195          200          205
Phe Arg Arg Ala Phe Ala Gly Ala Thr Val His Asp Phe Phe Asn Trp

```

240

210	215	220
Leu Ser Leu Leu Val	Leu Leu Pro Val	Glu Val Ala Thr His Tyr Leu
225	230	235
Glu Ile Ile Thr	Gln Leu Ile Val	Glu Ser Phe His Phe Lys Asn Gly
	245	250
Glu Asp Ala Pro Asp	Leu Leu Lys Val	Ile Thr Lys Pro Phe Thr Lys
	260	265
Leu Ile Val Gln	Leu Asp Lys Lys	Val Ile Ser Gln Ile Ala Met Asn
	275	280
Asp Glu Lys Ala Lys	Asn Lys Ser Leu Val	Lys Ile Trp Cys Lys Thr
290	295	300
Phe Thr Asn Lys Thr	Gln Ile Asn Val Thr	Val Pro Ser Thr Ala Asn
305	310	315
Cys Thr Ser Pro Ser	Leu Cys Trp Thr Asp	Gly Ile Gln Asn Trp Thr
	325	330
Met Lys Asn Val Thr	Tyr Lys Glu Asn Ile Ala	Lys Cys Gln His Ile
	340	345
Phe Val Asn Phe His	Ieu Pro Asp Leu Ala	Val Gly Thr Ile Leu Leu
	355	360
Ile Leu Ser Leu Leu	Val Leu Cys Gly Cys	Leu Ile Met Ile Val Lys
	370	375
Ile Leu Gly Ser Val	Leu Lys Gly Gln Val	Ala Thr Val Ile Lys Lys
385	390	395
Thr Ile Asn Thr Asp	Phe Pro Phe Pro Phe	Ala Trp Leu Thr Gly Tyr
	405	410
Leu Ala Ile Leu Val	Gly Ala Gly Met Thr	Phe Ile Val Gln Ser Ser
	420	425
Ser Val Phe Thr Ser	Ala Leu Thr Pro Leu	Ile Gly Ile Gly Val Ile
	435	440
Thr Ile Glu Arg Ala	Tyr Pro Leu Thr Leu	Gly Ser Asn Ile Gly Thr
	450	455
Thr Thr Thr Ala Ile	Leu Ala Ala Leu Ala	Ser Pro Gly Asn Ala Leu
465	470	475
Arg Ser Ser Leu Gln	Ile Ala Leu Cys His	Phe Phe Phe Asn Ile Ser
	485	490
Gly Ile Leu Leu Trp	Tyr Pro Ile Pro Phe	Thr Arg Leu Pro Ile Arg
	500	505
Met Ala Lys Gly Leu	Gly Asn Ile Ser Ala	Lys Tyr Arg Trp Phe Ala
	515	520
Val Phe Tyr Leu Ile	Ile Phe Phe Leu Ile	Pro Leu Thr Val Phe
	530	535
Gly Leu Ser Leu Ala	Gly Trp Arg Val Leu	Val Gly Val Gly Val Pro
545	550	555
Val Val Phe Ile Ile	Ile Ile Leu Val Leu	Cys Leu Arg Leu Leu Gln Ser
	565	570
Arg Cys Pro Arg Val	Leu Pro Lys Lys	Leu Gln Asn Trp Asn Phe Leu
	580	585
Pro Leu Trp Met Arg	Ser Leu Lys Pro Trp	Asp Ala Val Val Ser Lys
	595	600
Phe Thr Gly Cys Phe	Gln Met Arg Cys Cys	Cys Cys Cys Arg Val Cys
	610	615
Cys Arg Ala Cys Cys	Leu Leu Cys Gly Cys	Pro Lys Cys Cys Arg Cys
625	630	635
Ser Lys Cys Cys Glu	Asp Leu Glu Glu Ala	Gln Glu Gly Gln Asp Val
	645	650
Pro Val Lys Ala Pro	Glu Thr Phe Asp Asn	Ile Thr Ile Ser Arg Glu
	660	665
Ala Gln Gly Glu Val	Pro Ala Ser Asp Ser	Lys Thr Glu Cys Thr Ala

241

675                      680                      685  
 Leu

<210> 222  
 <211> 771  
 <212> DNA  
 <213> Homo sapiens

<400> 222  
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 gatccggatt caccattgtt cagagaagaa aactacgcct cagccctgag caatgtagta 180  
 acttttatgt ggaaaagtat ggaaaaatgt ttttcccaa cttaacagct tacatgagtt 240  
 ctggaccact tgtcgccatg atattagcta gacataaagc catctcttat tggtagaac 300  
 ttttgggacc aaataatagc ttagtagcga aggagacaca tccagacagt ctgagggcaa 360  
 tttatggcac agatgaccta aggaatgcac ttcattgggag taatgacttt gctgctgcgg 420  
 aaagagaaat acgttttatg tttcctgaag tgattgttga gccattcca attggacaag 480  
 ctgctaagga ctattttaa tttacatataa tgccaactct gcttgaagga ctcacagagc 540  
 tttgtaagca aaaaccagca gaccctttga tttggctagc tgattggctg ctgaaaaata 600  
 atcctaacaa acccaaactt tgtcaccatc caattgtaga agaaccttat taaaaaaaaa 660  
 atcctcgaaa gaacaaatca tgaactatct tattataaaa ggctgtactt ctactgtttg 720  
 agaaaattat ttctagggtt taagtaacta ccagtaaaat aaatttattt c 771

<210> 223  
 <211> 212  
 <212> PRT  
 <213> Homo sapiens

<400> 223  
 Met Glu Ile Ser Met Pro Pro Pro Gln Ile Tyr Val Glu Lys Thr Leu  
 1                      5                      10                      15  
 Ala Ile Ile Lys Pro Asp Ile Val Asp Lys Glu Glu Glu Ile Gln Asp  
 20                      25                      30  
 Ile Ile Leu Arg Ser Gly Phe Thr Ile Val Gln Arg Arg Lys Leu Arg  
 35                      40                      45  
 Leu Ser Pro Glu Gln Cys Ser Asn Phe Tyr Val Glu Lys Tyr Gly Lys  
 50                      55                      60  
 Met Phe Phe Pro Asn Leu Thr Ala Tyr Met Ser Ser Gly Pro Leu Val  
 65                      70                      75                      80  
 Ala Met Ile Leu Ala Arg His Lys Ala Ile Ser Tyr Trp Leu Glu Leu  
 85                      90                      95  
 Leu Gly Pro Asn Asn Ser Leu Val Ala Lys Glu Thr His Pro Asp Ser  
 100                      105                      110  
 Leu Arg Ala Ile Tyr Gly Thr Asp Leu Arg Asn Ala Leu His Gly  
 115                      120                      125  
 Ser Asn Asp Phe Ala Ala Ala Glu Arg Glu Ile Arg Phe Met Phe Pro  
 130                      135                      140  
 Glu Val Ile Val Glu Pro Ile Pro Ile Gly Gln Ala Ala Lys Asp Tyr  
 145                      150                      155                      160  
 Leu Asn Leu His Ile Met Pro Thr Leu Leu Glu Gly Leu Thr Glu Leu  
 165                      170                      175  
 Cys Lys Gln Lys Pro Ala Asp Pro Leu Ile Trp Leu Ala Asp Trp Leu  
 180                      185                      190  
 Leu Lys Asn Asn Pro Asn Lys Pro Lys Leu Cys His His Pro Ile Val  
 195                      200                      205  
 Glu Glu Pro Tyr

210

<210> 224  
<211> 3463  
<212> DNA  
<213> Homo sapiens

&lt;400&gt; 224

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gcaatgctgc cgccaccgcc accaccactt acgtcctcgc tccccgcagc cgggtcaaaag 180
ccttcctctg agtcgcagcc ccccatggag gccagtcctc tccccggggc tccgcccccc 240
ttcgacgccc agattcttcc cggggcgcaa ccccccttcg acgcccagtc tccccttgat 300
tctcagcctc aaccacagcg ccagccttgg aatttccatg cttccacatc gtggtattgg 360
agacagtctt ctgatagggt tcctcggcat cagaagtcct tcaaccctgc agttaaaaa 420
tcttattatc cacgaaagta tgatgcaaaa ttcacagact tcagcttacc tcccagtaga 480
aaacagaaaa aaaagaaaag aaaggaacca gtttttctact tttttgtga tactgtgat 540
cgtggtttta aaaatcaaga aaagtatgac aaacacatgt ctgaacatc aaaatgccct 600
gaattagatt gctcttttac tgcacacgag aagattgtcc agttccattg gagaaatag 660
catgctcctg gcatgaagaa gatcaagtta gacactccag aggaaattgc acggtggagg 720
gaagaaagaa ggaaaaacta tccaactctg gccaatattg aaaggaagaa gaagttaaaa 780
cttgaaggagg agaagagagg agcagtattg acaacaacac aatatggcaa gatgaagggg 840
atgtccagac attcacaagt ggcaaagatc agaagtcctg gcaagaatca caaatggaaa 900
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aacccttttt tccgtcaaaa ttggatttgt aattaattg taagcctcgt aggatgtatg 1620
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gttgatcccc aactgcctt aaggtatatt atagaaacag ttttattttc catttttctt 2940
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243

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gtttcctgat aataaatgta tttaggactg aaaatactcc tgagtactcc cctggctgta 3000
tgtctgacag tcttttagcta tggtgactat tgtttatttt taatgggtat ttcagattcc 3060
aagtgtatgtt aaaatttcta aggagatata atatagcctg tatggtttct actttatgga 3120
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gattattaaa acatttggac tattaaaaaa aaaaaaaaaa aaa 3463

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&lt;210&gt; 225

&lt;211&gt; 495

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 225

```

Met Ala Glu Pro Thr Ser Asp Phe Glu Thr Pro Ile Gly Trp His Ala
1 5 10 15
Ser Pro Glu Leu Thr Pro Thr Leu Gly Pro Leu Ser Asp Thr Ala Pro
20 25 30
Pro Arg Asp Arg Trp Met Phe Trp Ala Met Leu Pro Pro Pro Pro Pro
35 40 45
Pro Leu Thr Ser Ser Leu Pro Ala Ala Gly Ser Lys Pro Ser Ser Glu
50 55 60
Ser Gln Pro Pro Met Glu Ala Gln Ser Leu Pro Gly Ala Pro Pro Pro
65 70 75 80
Phe Asp Ala Gln Ile Leu Pro Gly Ala Gln Pro Pro Phe Asp Ala Gln
85 90 95
Ser Pro Leu Asp Ser Gln Pro Gln Pro Ser Gly Gln Pro Trp Asn Phe
100 105 110
His Ala Ser Thr Ser Trp Tyr Trp Arg Gln Ser Ser Asp Arg Phe Pro
115 120 125
Arg His Gln Lys Ser Phe Asn Pro Ala Val Lys Asn Ser Tyr Tyr Pro
130 135 140
Arg Lys Tyr Asp Ala Lys Phe Thr Asp Phe Ser Leu Pro Pro Ser Arg
145 150 155 160
Lys Gln Lys Lys Lys Lys Arg Lys Glu Pro Val Phe His Phe Phe Cys
165 170 175
Asp Thr Cys Asp Arg Gly Phe Lys Asn Gln Glu Lys Tyr Asp Lys His
180 185 190
Met Ser Glu His Thr Lys Cys Pro Glu Leu Asp Cys Ser Phe Thr Ala
195 200 205
His Glu Lys Ile Val Gln Phe His Trp Arg Asn Met His Ala Pro Gly
210 215 220
Met Lys Lys Ile Lys Leu Asp Thr Pro Glu Glu Ile Ala Arg Trp Arg
225 230 235 240
Glu Glu Arg Arg Lys Asn Tyr Pro Thr Leu Ala Asn Ile Glu Arg Lys
245 250 255
Lys Lys Leu Lys Leu Glu Lys Glu Lys Arg Gly Ala Val Leu Thr Thr
260 265 270
Thr Gln Tyr Gly Lys Met Lys Gly Met Ser Arg His Ser Gln Met Ala
275 280 285
Lys Ile Arg Ser Pro Gly Lys Asn His Lys Trp Lys Asn Asp Asn Ser
290 295 300
Arg Gln Arg Ala Val Thr Gly Ser Gly Ser His Leu Cys Asp Leu Lys
305 310 315 320
Leu Glu Gly Pro Pro Glu Ala Asn Ala Asp Pro Leu Gly Val Leu Ile
325 330 335

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244

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Asn Ser Asp Ser Glu Ser Asp Lys Glu Glu Lys Pro Gln His Ser Val
      340      345      350
Ile Pro Lys Glu Val Thr Pro Ala Leu Cys Ser Leu Met Ser Ser Tyr
      355      360      365
Gly Ser Leu Ser Gly Ser Glu Ser Glu Pro Glu Glu Thr Pro Ile Lys
      370      375      380
Thr Glu Ala Asp Val Leu Ala Glu Asn Gln Val Leu Asp Ser Ser Ala
      385      390      395      400
Pro Lys Ser Pro Ser Gln Asp Val Lys Ala Thr Val Arg Asn Phe Ser
      405      410      415
Glu Ala Lys Ser Glu Asn Arg Lys Lys Ser Phe Glu Lys Thr Asn Pro
      420      425      430
Lys Arg Lys Lys Asp Tyr His Asn Tyr Gln Thr Leu Phe Glu Pro Arg
      435      440      445
Thr His His Pro Tyr Leu Leu Glu Met Leu Leu Ala Pro Asp Ile Arg
      450      455      460
His Glu Arg Asn Val Ile Leu Gln Cys Val Arg Tyr Ile Ile Lys Lys
      465      470      475      480
Asp Phe Phe Gly Leu Asp Thr Asn Ser Ala Lys Ser Lys Asp Val
      485      490      495

```

<210> 226  
 <211> 942  
 <212> DNA  
 <213> Homo sapiens

```

<400> 226
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gccacatggc taaaccctga cccatctcag aagcagaatc tcttagcccc acagaatgct 180
gtgtcctctg aagaaaccaa tgactttaaa caagagacct ttccaagtaa gtccaacgaa 240
agccatgacc acatggatga tatggatgat gaagatgatg atgaccatgt ggacagccag 300
gactccattg actcgaacga ctctgatgat gtagatgaca ctgatgattc tcaccagtct 360
gatgagtctc accattctga tgaatctgat gaactgggtca ctgattttcc cacggacctg 420
ccagcaacog aagttttcac tccagttgtc cccacagtag acacatatga tggccgaggt 480
gatagtgtgg tttatggact gaggtcaaaa tctaagaagt ttgcgagacc tgacatccag 540
taccctgatg ctacagacga gcacatcacc tcacacatgg aaagcgagga gttgaatggt 600
gcatacaagg ccatccccgt tgcccaggac ctgaacgcgc cttctgattg ggacagccgt 660
gggaaggaca gttatgaaac gagtcagctg gatgaccaga gtgctgaagc ccacagccac 720
aagcagtcca gattatataa gcggaagct aatgatgaga gcaatgagca ttccgatgtg 780
attgatagtc aggaactttc caaagtcagc cgtgaattcc acagccatga atttcacagc 840
catgaagata tgctggttgt agaccccaaa agtaaggaag aagataaaca cctgaaattt 900
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<210> 227  
 <211> 314  
 <212> PRT  
 <213> Homo sapiens

```

<400> 227
Met Arg Ile Ala Val Ile Cys Phe Cys Leu Leu Gly Ile Thr Cys Ala
  1      5      10      15
Ile Pro Val Lys Gln Ala Asp Ser Gly Ser Ser Glu Glu Lys Gln Leu
      20      25      30
Tyr Asn Lys Tyr Pro Asp Ala Val Ala Thr Trp Leu Asn Pro Asp Pro
      35      40      45
Ser Gln Lys Gln Asn Leu Leu Ala Pro Gln Asn Ala Val Ser Ser Glu

```

245

50		55		60
Glu Thr Asn Asp Phe Lys Gln Glu Thr Leu Pro Ser Lys Ser Asn Glu				
65	70	75	80	
Ser His Asp His Met Asp Asp Met Asp Glu Asp Asp Asp Asp His				
	85	90	95	
Val Asp Ser Gln Asp Ser Ile Asp Ser Asn Asp Ser Asp Asp Val Asp				
	100	105	110	
Asp Thr Asp Asp Ser His Gln Ser Asp Glu Ser His His Ser Asp Glu				
	115	120	125	
Ser Asp Glu Leu Val Thr Asp Phe Pro Thr Asp Leu Pro Ala Thr Glu				
	130	135	140	
Val Phe Thr Pro Val Val Pro Thr Val Asp Thr Tyr Asp Gly Arg Gly				
145	150	155	160	
Asp Ser Val Val Tyr Gly Leu Arg Ser Lys Ser Lys Lys Phe Arg Arg				
	165	170	175	
Pro Asp Ile Gln Tyr Pro Asp Ala Thr Asp Glu His Ile Thr Ser His				
	180	185	190	
Met Glu Ser Glu Glu Leu Asn Gly Ala Tyr Lys Ala Ile Pro Val Ala				
	195	200	205	
Gln Asp Leu Asn Ala Pro Ser Asp Trp Asp Ser Arg Gly Lys Asp Ser				
	210	215	220	
Tyr Glu Thr Ser Gln Leu Asp Asp Gln Ser Ala Glu Ala His Ser His				
225	230	235	240	
Lys Gln Ser Arg Leu Tyr Lys Arg Lys Ala Asn Asp Glu Ser Asn Glu				
	245	250	255	
His Ser Asp Val Ile Asp Ser Gln Glu Leu Ser Lys Val Ser Arg Glu				
	260	265	270	
Phe His Ser His Glu Phe His Ser His Glu Asp Met Leu Val Val Asp				
	275	280	285	
Pro Lys Ser Lys Glu Glu Asp Lys His Leu Lys Phe Arg Ile Ser His				
	290	295	300	
Glu Leu Asp Ser Ala Ser Ser Glu Val Asn				
305	310			

&lt;210&gt; 228

&lt;211&gt; 1524

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 228

```

gcagagcaca gcatcgtcgg gaccagactc gtctcaggcc agttgcagcc ttctcagcca 60
aacgccgacc aaggaaaact cactaccatg agaattgcag tgatttgctt ttgcctccta 120
ggcatcacct gtgccatacc agttaaacag gctgattctg gaagttctga ggaaaagcag 180
ctttacaaca aatacccaga tgctgtggcc acatggctaa accctgaocc atctcagaag 240
cagaatctcc tagccccaca gacccttcca agtaagtcca acgaaagcca tgaccacatg 300
gatgatatgg atgatgaaga tgatgatgac catgtggaca gccaggactc cattgactcg 360
aacgactctg atgatgtaga tgacactgat gattctcacc agtctgatga gtctcaccat 420
tctgatgaat ctgatgaact ggtcactgat tttcccacgg acctgccagc aaccgaagtt 480
ttcactccag ttgtccccac agtagacaca tatgatggcc gaggtgatag tgtggtttat 540
ggactgaggt caaaatctaa gaagtttcgc agacctgaca tccagtaccc tgatgctaca 600
gacgaggaca tcacctcaca catggaaage gaggagttag atggtgcata caaggccatc 660
cccgttgccc aggacctgaa cgcgccttct gattgggaca gccgtgggaa ggacagttat 720
gaaacgagtc agctggatga ccagagtgtt gaaaccaca gccacaagca gtccagatta 780
tataagcggg aagccaatga tgagagcaat gacgattccg atgtgattga tagtcaggaa 840
ctttccaaag tcagccgtga attccacagc catgaatttc acagccatga agatagctg 900
gtttagagacc ccaaagtaa ggaagaagat aaacacctga aatttcgtat ttctcatgaa 960
ttagatagtg catcttctga ggtcaattaa aaggagaaaa aatacaattt ctactttgc 1020

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246

```

atttagtcaa aagaaaaaat gctttatagc aaaatgaaag agaacatgaa atgcttcttt 1080
ctcagtttat tgggttgaatg tgtatctatt tgagtctgga aataactaat gtgtttgata 1140
attagtttag tttgtggcct catggaaact ccctgtaaac taaaagcttc agggttatgt 1200
ctatgttcat tctatagaag aaatgcaaac tatcactgta ttttaatat ttgtattctc 1260
tcatgaatag aaatttatgt agaagcaaac aaaatacttt taccactta aaaagagaat 1320
ataacatttt atgtcactat aatcttttgt tttttaagtt agtgtatatt ttgttgtgat 1380
tatctttttg tgggtgtgaat aaatctttta tcttgaatgt aataagaatt tgggtggtgc 1440
aattgcttat ttgttttccc acggttgtcc agcaattaat aaaacataac cttttttact 1500
gcctaaaaaa aaaaaaaaaa aaaa                                     1524

```

&lt;210&gt; 229

&lt;211&gt; 300

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 229

```

Met Arg Ile Ala Val Ile Cys Phe Cys Leu Leu Gly Ile Thr Cys Ala
 1          5          10          15
Ile Pro Val Lys Gln Ala Asp Ser Gly Ser Ser Glu Glu Lys Gln Leu
 20          25          30
Tyr Asn Lys Tyr Pro Asp Ala Val Ala Thr Trp Leu Asn Pro Asp Pro
 35          40          45
Ser Gln Lys Gln Asn Leu Leu Ala Pro Gln Thr Leu Pro Ser Lys Ser
 50          55          60
Asn Glu Ser His Asp His Met Asp Asp Met Asp Asp Glu Asp Asp Asp
 65          70          75          80
Asp His Val Asp Ser Gln Asp Ser Ile Asp Ser Asn Asp Ser Asp Asp
 85          90          95
Val Asp Asp Thr Asp Asp Ser His Gln Ser Asp Glu Ser His His Ser
100          105          110
Asp Glu Ser Asp Glu Leu Val Thr Asp Phe Pro Thr Asp Leu Pro Ala
115          120          125
Thr Glu Val Phe Thr Pro Val Val Pro Thr Val Asp Thr Tyr Asp Gly
130          135          140
Arg Gly Asp Ser Val Val Tyr Gly Leu Arg Ser Lys Ser Lys Lys Phe
145          150          155          160
Arg Arg Pro Asp Ile Gln Tyr Pro Asp Ala Thr Asp Glu Asp Ile Thr
165          170          175
Ser His Met Glu Ser Glu Glu Leu Asn Gly Ala Tyr Lys Ala Ile Pro
180          185          190
Val Ala Gln Asp Leu Asn Ala Pro Ser Asp Trp Asp Ser Arg Gly Lys
195          200          205
Asp Ser Tyr Glu Thr Ser Gln Leu Asp Asp Gln Ser Ala Glu Thr His
210          215          220
Ser His Lys Gln Ser Arg Leu Tyr Lys Arg Lys Ala Asn Asp Glu Ser
225          230          235          240
Asn Glu His Ser Asp Val Ile Asp Ser Gln Glu Leu Ser Lys Val Ser
245          250          255
Arg Glu Phe His Ser His Glu Phe His Ser His Glu Asp Met Leu Val
260          265          270
Val Asp Pro Lys Ser Lys Glu Glu Asp Lys His Leu Lys Phe Arg Ile
275          280          285
Ser His Glu Leu Asp Ser Ala Ser Ser Glu Val Asn
290          295          300

```

&lt;210&gt; 230

&lt;211&gt; 861

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 230

```

atgagaattg cagtgatttg cttttgcctc ctaggcatca cctgtgccat accagttaaa 60
caggctgatt ctggaagttc tgaggaaaag cagaatgctg tgcctctga agaaaccaat 120
gactttaaac aagagaccct tccaagtaag tccaacgaaa gccatgacca catggatgat 180
atggatgatg aagatgatga tgaccatgtg gacagccagg actccattga ctggaacgac 240
tctgatgatg tagatgacac tgatgattct caccagtctg atgagtctca ccattctgat 300
gaatctgatg aactgggtcac tgattttccc acggacctgc cagcaaccga agttttcact 360
ccagttgtcc ccacagtaga cacatatgat ggccgaggtg atagtgtggt ttatggactg 420
aggtcaaaat ctaagaagtt tcgcagacct gacatccagt accctgatgc tacagacgag 480
cacatcacct cacacatgga aagcgaggag ttgaatggtg catacaaggc catccccgtt 540
gcccaggacc tgaacgcgcc ttctgattgg gacagccgtg ggaaggacag ttatgaaacg 600
agtcagctgg atgaccagag tgctgaagcc cacagccaca agcagtccag attatataag 660
cggaaagcta atgatgagag caatgagcat tccgatgtga ttgatagtca ggaactttcc 720
aaagtcagcc gtgaattcca cagccatgaa ttacacagcc atgaayatat gctgggttga 780
gaccccaaaa gtaagggaaga agataaacac ctgaaatttc gtatttctca tgaattagat 840
agtgcattct ctgaggtcaa t                                     861

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&lt;210&gt; 231

&lt;211&gt; 287

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 231

```

Met Arg Ile Ala Val Ile Cys Phe Cys Leu Leu Gly Ile Thr Cys Ala
 1             5             10             15
Ile Pro Val Lys Gln Ala Asp Ser Gly Ser Ser Glu Glu Lys Gln Asn
      20             25             30
Ala Val Ser Ser Glu Glu Thr Asn Asp Phe Lys Gln Glu Thr Leu Pro
      35             40             45
Ser Lys Ser Asn Glu Ser His Asp His Met Asp Asp Met Asp Asp Glu
      50             55             60
Asp Asp Asp Asp His Val Asp Ser Gln Asp Ser Ile Asp Ser Asn Asp
      65             70             75             80
Ser Asp Asp Val Asp Asp Thr Asp Asp Ser His Gln Ser Asp Glu Ser
      85             90             95
His His Ser Asp Glu Ser Asp Glu Leu Val Thr Asp Phe Pro Thr Asp
      100            105            110
Leu Pro Ala Thr Glu Val Phe Thr Pro Val Val Pro Thr Val Asp Thr
      115            120            125
Tyr Asp Gly Arg Gly Asp Ser Val Val Tyr Gly Leu Arg Ser Lys Ser
      130            135            140
Lys Lys Phe Arg Arg Pro Asp Ile Gln Tyr Pro Asp Ala Thr Asp Glu
      145            150            155            160
His Ile Thr Ser His Met Glu Ser Glu Glu Leu Asn Gly Ala Tyr Lys
      165            170            175
Ala Ile Pro Val Ala Gln Asp Leu Asn Ala Pro Ser Asp Trp Asp Ser
      180            185            190
Arg Gly Lys Asp Ser Tyr Glu Thr Ser Gln Leu Asp Asp Gln Ser Ala
      195            200            205
Glu Ala His Ser His Lys Gln Ser Arg Leu Tyr Lys Arg Lys Ala Asn
      210            215            220
Asp Glu Ser Asn Glu His Ser Asp Val Ile Asp Ser Gln Glu Leu Ser
      225            230            235            240
Lys Val Ser Arg Glu Phe His Ser His Glu Phe His Ser His Glu Asp
      245            250            255

```

248

Met Leu Val Val Asp Pro Lys Ser Lys Glu Glu Asp Lys His Leu Lys  
                   260                  265                  270  
 Phe Arg Ile Ser His Glu Leu Asp Ser Ala Ser Ser Glu Val Asn  
                   275                  280                  285

<210> 232  
 <211> 838  
 <212> DNA  
 <213> Homo sapiens

<400> 232  
 ctcagagcca cccacagccg cagccatgct gtgcctcctg ctcaccctgg gcgtggccct 60  
 ggtctgtggt gtcccgccca tggacatccc ccagaccaag caggacctgg agctcccaa 120  
 gttggcaggg acctggcact ccatggccat ggcgaccaac aacatctccc tcatggcgac 180  
 actgaaggcc cctctgaggg tccacatcac ctactgttg cccacccccg aggacaacct 240  
 ggagatcggt ctgcacagat gggagaacaa cagctgtgtt gagaagaagg tccttggaga 300  
 gaagactgag aatccaaaga agttcaagat caactatacg gtggcgaacg aggccacgct 360  
 gctcgatact gactacgaca atttcctgtt tctctgccta caggacacca ccacccccat 420  
 ccagagcatg atgtgccagt acctggccag agtccctggtg gaggacgatg agatcatgca 480  
 gggattcatc agggctttca ggcccctgcc caggcaccta tggacttgct tggacttgaa 540  
 acagatggaa gagccgtgcc gtttctaggt gagctcctgc ctggtcctgc ctctggctc 600  
 acctccgcct ccaggaagac cagactccca cccttcaca cctccagagc agtgggactt 660  
 cctcctgccc ttccaaagaa taaccacagc tcagaagacg atgacgtggt catctgtgtc 720  
 gccatcccct tcctgctgca cacctgcacc acggccatgg ggaggctgct ccctgggggc 780  
 agagtctctg gcagaggtta ttaataaacc cttggagcat gaaaaaaaa aaaaaaaa 838

<210> 233  
 <211> 180  
 <212> PRT  
 <213> Homo sapiens

<400> 233  
 Met Leu Cys Leu Leu Leu Thr Leu Gly Val Ala Leu Val Cys Gly Val  
   1                  5                  10                  15  
 Pro Ala Met Asp Ile Pro Gln Thr Lys Gln Asp Leu Glu Leu Pro Lys  
                   20                  25                  30  
 Leu Ala Gly Thr Trp His Ser Met Ala Met Ala Thr Asn Asn Ile Ser  
                   35                  40                  45  
 Leu Met Ala Thr Leu Lys Ala Pro Leu Arg Val His Ile Thr Ser Leu  
   50                  55                  60  
 Leu Pro Thr Pro Glu Asp Asn Leu Glu Ile Val Leu His Arg Trp Glu  
   65                  70                  75                  80  
 Asn Asn Ser Cys Val Glu Lys Lys Val Leu Gly Glu Lys Thr Glu Asn  
                   85                  90                  95  
 Pro Lys Lys Phe Lys Ile Asn Tyr Thr Val Ala Asn Glu Ala Thr Leu  
                   100                  105                  110  
 Leu Asp Thr Asp Tyr Asp Asn Phe Leu Phe Leu Cys Leu Gln Asp Thr  
                   115                  120                  125  
 Thr Thr Pro Ile Gln Ser Met Met Cys Gln Tyr Leu Ala Arg Val Leu  
   130                  135                  140  
 Val Glu Asp Asp Glu Ile Met Gln Gly Phe Ile Arg Ala Phe Arg Pro  
   145                  150                  155                  160  
 Leu Pro Arg His Leu Trp Tyr Leu Leu Asp Leu Lys Gln Met Glu Glu  
                   165                  170                  175  
 Pro Cys Arg Phe  
                   180

<210> 234  
 <211> 851  
 <212> DNA  
 <213> Homo sapiens

<400> 234  
 ggctccagag ctcagagcca cccacagccg cagccatgct gtgcctcctg ctcaccctgg 60  
 gcgtggccct ggtctgtggt gtcccggcca tggacatccc ccagaccaag caggacctgg 120  
 agctcccaaa gttggcaggg acctggcact ccatggccat ggcgaccaac aacatctccc 180  
 tcatggcgac actgaaggcc cctctgaggg tccacatcac ctactgttg cccacccccg 240  
 aggacaacct ggagatcggt ctgcacagat gggagaacaa cagctgtgtt gagaagaagg 300  
 tccttgagaga gaagactgag aatccaaaga agttcaagat caactatacg gtggcgaacg 360  
 aggccacgct gctcgatact gactacgaca atttctgtt tctctgccta caggacacca 420  
 ccacccccat ccagagcatg atgtgccagt acctggccag agtcctggtg gaggacgatg 480  
 agatcatgca gggattcatc agygctttca gggccctgcc caggcaccta tggtagttgc 540  
 tggacttgaa acagatggaa gagccgtgcc gtttctaggt gagctcctgc ctggtcctgc 600  
 ctctgggtg acctgtaaac ccaacagctc acctccgct ccaggaagac cagactccca 660  
 cccttcacac cctccagagc agtgggactt cctcctgccc ttcaaagaa taaccacagc 720  
 tcagaagacg atgacgtggt catctgtgtc gccatcccc tctgtctgca cacctgcacc 780  
 acggccatgg ggaggctgct ccctgggggc agagtctctg gcagaggtta ttaataaacc 840  
 cttggagcat g 851

<210> 235  
 <211> 811  
 <212> DNA  
 <213> Homo sapiens

<400> 235  
 catccctctg gctccagagc tcagagccac ccacagccgc agccatgctg tgcctcctgc 60  
 tcaccctggg cgtggccctg gtctgtggtg tcccggccat ggacatcccc cagaccaagc 120  
 aggacctgga gctcccaaag ttggcagggg cctggcactc catggccatg gcgaccaaca 180  
 acatctccct catggcgaca ctgaaggccc ctctgagggg ccacatcacc tcaactgttg 240  
 ccacccccga ggacaacctg gagatcggtc tgacacagat ggagaacaac agctgtgttg 300  
 agaagaaggt ccttgagag aagactggga atccaaagaa gttcaagatc aactatacgg 360  
 tggcgaacga ggccacgctg ctcgatactg actacgacaa tttcctgttt ctctgcctac 420  
 aggacaccac ccccccatc cagagcatga tgtgccagta cctggccaga gtccctggtg 480  
 aggacgatga gatcatgcag ggattcatca gggctttcag gccctgccg aggcacctat 540  
 ggtacttgct ggacttgaaa cagatggaag agccgtgccg tttctagctc acctccgctc 600  
 ccaggaagac cagactccca cccttcacac cctccagagc agtgggactt cctcctgccc 660  
 tttcaaagaa taaccacagc tcagaagacg atgacgtggt catctgtgtc gccatcccc 720  
 tctgtctgca cacctgcacc attgccatgg ggaggctgct ccctgggggc agagtctctg 780  
 gcagaggtta ttaataaacc cttggagcat g 811

<210> 236  
 <211> 850  
 <212> DNA  
 <213> Homo sapiens

<400> 236  
 catccctctg gctccagagc tcagagccac ccacagccgc agccatgctg tgcctcctgc 60  
 tcaccctggg cgtggccctg gtctgtggtg tcccggccat ggacatcccc cagaccaagc 120  
 aggacctgga gctcccaaag ttggcagggg cctggcactc catggccatg gcgaccaaca 180  
 acatctccct catggcgaca ctgaaggccc ctctgagggg ccacatcacc tcaactgttg 240  
 ccacccccga ggacaacctg gagatcggtc tgacacagat ggagaacaac agctgtgttg 300  
 agaagaaggt ccttgagag aagactgrga atccaaagaa gttcaagatc aactatacgg 360  
 tggcgaacga ggccacgctg ctcgatactg actacgacaa tttcctgttt ctctgcctac 420  
 aggacaccac ccccccatc cagagcatga tgtgccagta cctggccaga gtccctggtg 480

250

```

aggacgatga gatcatgcag ggattcatca gggctttcag gccctgccc aggcacctat 540
ggtacttgct ggacttgaaa cagatggaag agccgtgccg tttctagtga cctgtaaacc 600
caacagctca cctccgcctc caggaagacc agactccac ccttccacac ctccagagca 660
gtgggacttc ctcctgccct ttcaaagaat aaccacagct cagaagacga tgacgtggtc 720
atctgtgtcg ccatcccctt cctgctgcac acctgcacca cggccatggg gaggtgctc 780
cctgggggca gagtctctgg cagaggttat taataaacc ttggagcatg aaaaaaaaaa 840
aaaaaaaaa                                     850

```

<210> 237  
 <211> 598  
 <212> DNA  
 <213> Homo sapiens

```

<400> 237
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tcaccctggg cgtggccctg gtctgtggtg tcccgccat ggacatcccc cagaccaagc 120
aggacctgga gctccaaaag gacaccacca ccccatcca gagcatgatg tgccagtacc 180
tgccagagt cctgggtggag gacgatgaga tcatgcaggg attcatcagg gctttcaggc 240
ccctgcccag gcacctatgg tacttgctgg acttgaaaca gatggaagag ccgtgccgtt 300
tctaggtgag ctctgcctg gtctgcctc ctgggtgacc tgtaaaccac acagctcacc 360
tccgcctcca ggaagaccag actcccaccc ttccacacct ccagagcagt gggacttcct 420
cctgcccttt caaagaataa ccacagctca gaagacgatg acgtgggtcat ctgtgtcgcc 480
atccccttcc tgctgcacac ctgcaccacg gccatgggga ggctgctccc tgggggcaga 540
gtctctggca gaggttatta ataaaccctt ggagcatgaa aaaaaaaaaa aaaaaaaa 598

```

<210> 238  
 <211> 86  
 <212> PRT  
 <213> Homo sapiens

```

<400> 238
Met Leu Cys Leu Leu Thr Leu Gly Val Ala Leu Val Cys Gly Val
 1             5             10            15
Pro Ala Met Asp Ile Pro Gln Thr Lys Gln Asp Leu Glu Leu Pro Lys
      20             25             30
Asp Thr Thr Thr Pro Ile Gln Ser Met Met Cys Gln Tyr Leu Ala Arg
      35             40             45
Val Leu Val Glu Asp Asp Glu Ile Met Gln Gly Phe Ile Arg Ala Phe
      50             55             60
Arg Pro Leu Pro Arg His Leu Trp Tyr Leu Leu Asp Leu Lys Gln Met
      65             70             75             80
Glu Glu Pro Cys Arg Phe
              85

```

<210> 239  
 <211> 814  
 <212> DNA  
 <213> Homo sapiens

```

<400> 239
catccctctg gctccagagc tcagagccac ccacagccgc agccatgctg tgcctcctgc 60
tcaccctggg cgtggccctg gtctgtggtg tcccgccat ggacatcccc cagaccaagc 120
aggacctgga gacactgaag gccctctga gggccacat cacctcactg ttgccaccc 180
ccgaggacaa cctggagatc gttctgcaca gatgggagaa caacagctgt gttgagaaga 240
aggtccttgg agagaagact grgaatccaa agaagttcaa gatcaactat acggtggcga 300
acgaggccac gctgctcgat actgactacg acaatttctt gtttctctgc ctacaggaca 360
ccaccacccc catccagagc atgatgtgcc agtacctggc cagagtctctg gtggaggacg 420

```

251

```

atgagatcat gcagggattc atcagggcct tcaggcccct gccagggcac ctatgggtact 480
tgctggactt gaaacagatg gaagagccgt gccgtttcta ggtgagctcc tgcctgggtcc 540
tgctcctcctg gtgacctgta aacccaacag ctcacctccg cctccaggaa gaccagactc 600
ccacccttcc acacctccag agcagtggga cttcctcctg ccctttcaaa gaataaccac 660
agctcagaag acgatgacgt ggatcatctgt gtcgccatcc ccttcctgct gcacacctgc 720
accacggcca tggggaggct gctccctggg ggcagagtct ctggcagagg ttattaataa 780
acccttgag catgaaaaaa aaaaaaaaaa aaaa 814

```

&lt;210&gt; 240

&lt;211&gt; 158

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 240

```

Met Leu Cys Leu Leu Thr Leu Gly Val Ala Leu Val Cys Gly Val
 1          5          10          15
Pro Ala Met Asp Ile Pro Gln Thr Lys Gln Asp Leu Glu Leu Pro Lys
 20          25          30
Ala Pro Leu Arg Val His Ile Thr Ser Leu Leu Pro Thr Pro Glu Asp
 35          40          45
Asn Leu Glu Ile Val Leu His Arg Trp Glu Asn Asn Ser Cys Val Glu
 50          55          60
Lys Lys Val Leu Gly Glu Lys Thr Glu Asn Pro Lys Lys Phe Lys Ile
 65          70          75          80
Asn Tyr Thr Val Ala Asn Glu Ala Thr Leu Leu Asp Thr Asp Tyr Asp
 85          90          95
Asn Phe Leu Phe Leu Cys Leu Gln Asp Thr Thr Thr Pro Ile Gln Ser
 100          105          110
Met Met Cys Gln Tyr Leu Ala Arg Val Leu Val Glu Asp Asp Glu Ile
 115          120          125
Met Gln Gly Phe Ile Arg Ala Phe Arg Pro Leu Pro Arg His Leu Trp
 130          135          140
Tyr Leu Leu Asp Leu Lys Gln Met Glu Glu Pro Cys Arg Phe
 145          150          155

```

&lt;210&gt; 241

&lt;211&gt; 158

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 241

```

Met Leu Cys Leu Leu Thr Leu Gly Val Ala Leu Val Cys Gly Val
 1          5          10          15
Pro Ala Met Asp Ile Pro Gln Thr Lys Gln Asp Leu Glu Thr Leu Lys
 20          25          30
Ala Pro Leu Arg Val His Ile Thr Ser Leu Leu Pro Thr Pro Glu Asp
 35          40          45
Asn Leu Glu Ile Val Leu His Arg Trp Glu Asn Asn Ser Cys Val Glu
 50          55          60
Lys Lys Val Leu Gly Glu Lys Thr Glu Asn Pro Lys Lys Phe Lys Ile
 65          70          75          80
Asn Tyr Thr Val Ala Asn Glu Ala Thr Leu Leu Asp Thr Asp Tyr Asp
 85          90          95
Asn Phe Leu Phe Leu Cys Leu Gln Asp Thr Thr Thr Pro Ile Gln Ser
 100          105          110
Met Met Cys Gln Tyr Leu Ala Arg Val Leu Val Glu Asp Asp Glu Ile
 115          120          125

```

252

Met Gln Gly Phe Ile Arg Ala Phe Arg Pro Leu Pro Arg His Leu Trp  
 130 135 140  
 Tyr Leu Leu Asp Leu Lys Gln Met Glu Glu Pro Cys Arg Phe  
 145 150 155

<210> 242  
 <211> 2707  
 <212> DNA  
 <213> Homo sapiens

<400> 242  
 ggcacgaggc ttcagaagga ggagagacac cgggccagg gcaccctcgc gggcgagacc 60  
 aagcagtggg ggcctgcagc cggccggcca gggcagcggc aggcgcggcc cggacctacg 120  
 ggaggaagcc ccgagccctc ggccggctgc gagcgactcc ccggcgatgc ctcacaactc 180  
 catcagatct ggccatggag ggctgaacca gctgggagg gcctttgtga atggcagacc 240  
 tctgccggaa gtggtccgcc agcgcacgt agacctggcc caccagggtg taaggccctg 300  
 cgacatctct cgccagctcc gcgtcagcca tggctgcgtc agcaagatcc ttggcaggta 360  
 ctacgagact ggcagcatcc ggcctggagt gatagggggc tccaagccca aggtggccac 420  
 ccccaaggty gtggagaaga ttggggacta caaacgccag aacctacca tgtttgcctg 480  
 ggagatccga gaccgcctcc tggctgaggc cgtctgtgac aatgacactg tgcccagtgt 540  
 cagctccatt aatagaatca tccggaccaaa agtgcagcaa ccattcaacc tccctatgga 600  
 cagctgcgtg gccaccaagt ccctgagtcc cggacacacg ctgatcccca gctcagctgt 660  
 aactcccccg gagtcacccc agtcggattc cctgggctcc acctactcca tcaatgggct 720  
 cctgggcatac gctcagcctg gcagcgacaa gaggaaaatg gatgacagt atcaggatag 780  
 ctgccgacta agcattgact cacagagcag cagcagcgga ccccgaaagc accttcgcac 840  
 ggatgccttc agccagcacc acctcgagcc gctcgagtgc ccatttgagc ggcagcacta 900  
 ccragaggcc tatgcctccc ccagccacac caaaggcgag cagggcctct acccgctgcc 960  
 cttgctcaac agcaccctgg acgacgggaa ggccaccctg accccttcca acacgccact 1020  
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 Leu Ser Thr His Gln Thr Tyr Pro Val Val Ala Asp Pro His Ser Pro  
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 Phe Ala Ile Lys Gln Glu Thr Pro Glu Val Ser Ser Ser Ser Thr  
 305 310 315 320  
 Pro Ser Ser Leu Ser Ser Ser Ala Phe Leu Asp Leu Gln Gln Val Gly  
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 Ser Gly Val Pro Pro Phe Asn Ala Phe Pro His Ala Ala Ser Val Tyr  
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 Pro Thr Leu Pro Gly Tyr Pro Pro His Ile Pro Thr Ser Gly Gln Gly  
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 Ser Gly Asn Ala Tyr Gly His Thr Pro Tyr Ser Ser Tyr Ser Glu Ala

254

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Trp	Arg	Phe	Pro	Asn	Ser	Ser	Leu	Leu	Ser	Ser	Pro	Tyr	Tyr	Tyr	Ser
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Ser	Thr	Ser	Arg	Pro	Ser	Ala	Pro	Pro	Thr	Thr	Ala	Thr	Ala	Phe	Asp
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His	Leu														
	450														

&lt;210&gt; 244

&lt;211&gt; 2381

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

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&lt;223&gt; n = A,T,C or G

&lt;400&gt; 244

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Arg 33	Ile 34	Val 35	Asp 36	Leu 37	Ala 38	His 39	Gln 40	Gly 41	Val 42	Arg 43	Pro 44	Cys 45	Asp 46	Ile 47	Ser 48
Arg 49	Gln 50	Leu 51	Arg 52	Val 53	Ser 54	His 55	Gly 56	Cys 57	Val 58	Ser 59	Lys 60	Ile 61	Leu 62	Gly 63	Arg 64
Tyr 65	Tyr 66	Glu 67	Thr 68	Gly 69	Ser 70	Ile 71	Arg 72	Pro 73	Gly 74	Val 75	Ile 76	Gly 77	Gly 78	Ser 79	Lys 80
Pro 81	Lys 82	Val 83	Ala 84	Thr 85	Pro 86	Lys 87	Val 88	Val 89	Glu 90	Lys 91	Ile 92	Gly 93	Asp 94	Tyr 95	Lys 96
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Asn 129	Arg 130	Ile 131	Ile 132	Arg 133	Thr 134	Lys 135	Val 136	Gln 137	Gln 138	Pro 139	Phe 140	Asn 141	Leu 142	Pro 143	Met 144
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Ser 193	Asp 194	Lys 195	Arg 196	Lys 197	Met 198	Asp 199	Asp 200	Ser 201	Asp 202	Gln 203	Asp 204	Ser 205	Cys 206	Arg 207	Leu 208
Ser 209	Ile 210	Asp 211	Ser 212	Gln 213	Ser 214	Ser 215	Ser 216	Ser 217	Gly 218	Pro 219	Arg 220	Lys 221	His 222	Leu 223	Arg 224
Thr 225	Asp 226	Ala 227	Phe 228	Ser 229	Gln 230	His 231	His 232	Leu 233	Glu 234	Pro 235	Leu 236	Glu 237	Cys 238	Pro 239	Phe 240
Glu 241	Arg 242	Gln 243	His 244	Tyr 245	Pro 246	Glu 247	Ala 248	Tyr 249	Ala 250	Ser 251	Pro 252	Ser 253	His 254	Thr 255	Lys 256
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Gly 305	Pro 306	Thr 307	Leu 308	Pro 309	Gly 310	Tyr 311	Pro 312	Pro 313	His 314	Ile 315	Pro 316	Thr 317	Ser 318	Gly 319	Gln 320
Gly 321	Ser 322	Tyr 323	Ala 324	Ser 325	Ser 326	Ala 327	Ile 328	Ala 329	Gly 330	Met 331	Val 332	Ala 333	Gly 334	Ser 335	Glu 336
Tyr 337	Ser 338	Gly 339	Asn 340	Ala 341	Tyr 342	Gly 343	His 344	Thr 345	Pro 346	Tyr 347	Ser 348	Ser 349	Tyr 350	Ser 351	Glu 352
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385

&lt;210&gt; 246

&lt;211&gt; 387

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 246

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          35          40          45
Arg Gln Leu Arg Val Ser His Gly Cys Val Ser Lys Ile Leu Gly Arg
          50          55          60
Tyr Tyr Glu Thr Gly Ser Ile Arg Pro Gly Val Ile Gly Gly Ser Lys
65          70          75          80
Pro Lys Val Ala Thr Pro Lys Val Val Glu Lys Ile Gly Asp Tyr Lys
          85          90          95
Arg Gln Asn Pro Thr Met Phe Ala Trp Glu Ile Arg Asp Arg Leu Leu
          100          105          110
Ala Glu Gly Val Cys Asp Asn Asp Thr Val Pro Ser Val Ser Ser Ile
          115          120          125
Asn Arg Ile Ile Arg Thr Lys Val Gln Gln Pro Phe Asn Leu Pro Met
          130          135          140
Asp Ser Cys Val Ala Thr Lys Ser Leu Ser Pro Gly His Thr Leu Ile
145          150          155          160
Pro Ser Ser Ala Val Thr Pro Pro Glu Ser Pro Gln Ser Asp Ser Leu
          165          170          175
Gly Ser Thr Tyr Ser Ile Asn Gly Leu Leu Gly Ile Ala Gln Pro Gly
          180          185          190
Ser Asp Lys Arg Lys Met Asp Asp Ser Asp Gln Asp Ser Cys Arg Leu
          195          200          205
Ser Ile Asp Ser Gln Ser Ser Ser Ser Gly Pro Arg Lys His Leu Arg
          210          215          220
Thr Asp Ala Phe Ser Gln His His Leu Glu Pro Leu Glu Cys Pro Phe
225          230          235          240
Glu Arg Gln His Tyr Pro Glu Ala Tyr Ala Ser Pro Ser His Thr Lys
          245          250          255
Gly Glu Gln Gly Leu Tyr Pro Leu Pro Leu Leu Asn Ser Thr Leu Asp
          260          265          270
Asp Gly Lys Ala Thr Leu Thr Pro Ser Asn Thr Pro Leu Gly Arg Asn
          275          280          285
Leu Ser Thr His Gln Thr Tyr Pro Val Val Ala Gly Arg Glu Met Val
          290          295          300
Gly Pro Thr Leu Pro Gly Tyr Pro Pro His Ile Pro Thr Ser Gly Gln
305          310          315          320
Gly Ser Tyr Ala Ser Ser Ala Ile Ala Gly Met Val Ala Gly Ser Glu
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Tyr Ser Gly Asn Ala Tyr Gly His Thr Pro Tyr Ser Ser Tyr Ser Glu
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Ala Trp Gly Phe Pro Asn Ser Ser Leu Leu Ser Ser Pro Tyr Tyr Tyr
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385

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258

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2641

&lt;210&gt; 248

&lt;211&gt; 398

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 248

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Arg Ile Val Asp Leu Ala His Gln Gly Val Arg Pro Cys Asp Ile Ser
      35          40          45
Arg Gln Leu Arg Val Ser His Gly Cys Val Ser Lys Ile Leu Gly Arg
      50          55          60
Tyr Tyr Glu Thr Gly Ser Ile Arg Pro Gly Val Ile Gly Gly Ser Lys
      65          70          75          80
Pro Lys Val Ala Thr Pro Lys Val Val Glu Lys Ile Gly Asp Tyr Lys
      85          90          95
Arg Gln Asn Pro Thr Met Phe Ala Trp Glu Ile Arg Asp Arg Leu Leu
      100          105          110
Ala Glu Gly Val Cys Asp Asn Asp Thr Val Pro Ser Val Ser Ser Ile
      115          120          125
Asn Arg Ile Ile Arg Thr Lys Val Gln Gln Pro Phe Asn Leu Pro Met
      130          135          140
Asp Ser Cys Val Ala Thr Lys Ser Leu Ser Pro Gly His Thr Leu Ile
      145          150          155          160
Pro Ser Ser Ala Val Thr Pro Pro Glu Ser Pro Gln Ser Asp Ser Leu
      165          170          175
Gly Ser Thr Tyr Ser Ile Asn Gly Leu Leu Gly Ile Ala Gln Pro Gly
      180          185          190
Ser Asp Lys Arg Lys Met Asp Asp Ser Asp Gln Asp Ser Cys Arg Leu
      195          200          205
Ser Ile Asp Ser Gln Ser Ser Ser Ser Gly Pro Arg Lys His Leu Arg
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Thr Asp Ala Phe Ser Gln His His Leu Glu Pro Leu Glu Cys Pro Phe
      225          230          235          240
Glu Arg Gln His Tyr Pro Glu Ala Tyr Ala Ser Pro Ser His Thr Lys
      245          250          255
Gly Glu Gln Gly Leu Tyr Pro Leu Pro Leu Leu Asn Ser Thr Leu Asp
      260          265          270
Asp Gly Lys Ala Thr Leu Thr Pro Ser Asn Thr Pro Leu Gly Arg Asn
      275          280          285
Leu Ser Thr His Gln Thr Tyr Pro Val Val Ala Ala Pro Pro Phe Trp
      290          295          300
Ile Cys Ser Lys Ser Ala Pro Gly Ser Arg Pro Ser Met Pro Phe Pro
      305          310          315          320
Met Leu Pro Pro Cys Thr Gly Ser Ser Arg Ala Arg Pro Ser Ser Gln
      325          330          335
Gly Glu Arg Trp Trp Gly Pro Arg Cys Pro Asp Thr His Pro Thr Ser
      340          345          350
Pro Pro Ala Asp Arg Ala Ala Met Pro Pro Leu Pro Ser Gln Ala Trp
      355          360          365
Trp Gln Glu Val Asn Thr Leu Ala Met Pro Met Ala Thr Pro Pro Thr
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Pro Pro Thr Ala Arg Pro Gly Ala Ser Pro Thr Pro Ala Cys
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259

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aaaaaaaaaa 2410

<210> 250  
<211> 321  
<212> PRT

260

&lt;213&gt; Homo sapiens

&lt;400&gt; 250

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Gly Gly Ala Phe Val Asn Gly Arg Pro Leu Pro Glu Val Val Arg Gln
      20           25           30
Arg Ile Val Asp Leu Ala His Gln Gly Val Arg Pro Cys Asp Ile Ser
      35           40           45
Arg Gln Leu Arg Val Ser His Gly Cys Val Ser Lys Ile Leu Gly Arg
 50           55           60
Tyr Tyr Glu Thr Gly Ser Ile Arg Pro Gly Val Ile Gly Gly Ser Lys
65           70           75           80
Pro Lys Val Ala Thr Pro Lys Val Val Glu Lys Ile Gly Asp Tyr Lys
      85           90           95
Arg Gln Asn Pro Thr Met Phe Ala Trp Glu Ile Arg Asp Arg Leu Leu
      100          105          110
Ala Glu Gly Val Cys Asp Asn Asp Thr Val Pro Ser Val Ser Ser Ile
      115          120          125
Asn Arg Ile Ile Arg Thr Lys Val Gln Gln Pro Phe Asn Leu Pro Met
      130          135          140
Asp Ser Cys Val Ala Thr Lys Ser Leu Ser Pro Gly His Thr Leu Ile
145          150          155          160
Pro Ser Ser Ala Val Thr Pro Pro Glu Ser Pro Gln Ser Asp Ser Leu
      165          170          175
Gly Ser Thr Tyr Ser Ile Asn Gly Leu Leu Gly Ile Ala Gln Pro Gly
      180          185          190
Ser Asp Lys Arg Lys Met Asp Asp Ser Asp Gln Asp Ser Cys Arg Leu
      195          200          205
Ser Ile Asp Ser Gln Ser Ser Ser Ser Gly Pro Arg Lys His Leu Arg
      210          215          220
Thr Asp Ala Phe Ser Gln His His Leu Glu Pro Leu Glu Cys Pro Phe
225          230          235          240
Glu Arg Gln His Tyr Pro Glu Ala Tyr Ala Ser Pro Ser His Thr Lys
      245          250          255
Gly Glu Gln Gly Glu Arg Trp Trp Gly Pro Arg Cys Pro Asp Thr His
      260          265          270
Pro Thr Ser Pro Pro Ala Asp Arg Ala Ala Met Pro Pro Leu Pro Ser
      275          280          285
Gln Ala Trp Trp Gln Glu Val Asn Thr Leu Ala Met Pro Met Ala Thr
      290          295          300
Pro Pro Thr Pro Pro Thr Ala Arg Pro Gly Ala Ser Pro Thr Pro Ala
305          310          315          320
Cys

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&lt;210&gt; 251

&lt;211&gt; 2308

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

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&lt;400&gt; 251

261

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aaaaaaaaa aaaaaaaaaa aaaaaaaa 2308

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&lt;210&gt; 252

&lt;211&gt; 287

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 252

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Met Pro His Asn Ser Ile Arg Ser Gly His Gly Gly Leu Asn Gln Leu
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Gly Gly Ala Phe Val Asn Gly Arg Pro Leu Pro Glu Val Val Arg Gln
20           25           30
Arg Ile Val Asp Leu Ala His Gln Gly Val Arg Pro Cys Asp Ile Ser
35           40           45
Arg Gln Leu Arg Val Ser His Gly Cys Val Ser Lys Ile Leu Gly Arg
50           55           60
Tyr Tyr Glu Thr Gly Ser Ile Arg Pro Gly Val Ile Gly Gly Ser Lys
65           70           75           80
Pro Lys Val Ala Thr Pro Lys Val Val Glu Lys Ile Gly Asp Tyr Lys
85           90           95

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262

Arg Gln Asn Pro Thr Met Phe Ala Trp Glu Ile Arg Asp Arg Leu Leu  
                   100                  105                  110  
 Ala Glu Gly Val Cys Asp Asn Asp Thr Val Pro Ser Val Ser Ser Ile  
                   115                  120                  125  
 Asn Arg Ile Ile Arg Thr Lys Val Gln Gln Pro Phe Asn Leu Pro Met  
                   130                  135                  140  
 Asp Ser Cys Val Ala Thr Lys Ser Leu Ser Pro Gly His Thr Leu Ile  
                   145                  150                  155                  160  
 Pro Ser Ser Ala Val Thr Pro Pro Glu Ser Pro Gln Ser Asp Ser Leu  
                   165                  170                  175  
 Gly Ser Thr Tyr Ser Ile Asn Gly Leu Leu Gly Ile Ala Gln Pro Gly  
                   180                  185                  190  
 Ser Asp Lys Arg Lys Met Asp Asp Ser Asp Gln Asp Ser Cys Arg Leu  
                   195                  200                  205  
 Ser Ile Asp Ser Gln Ser Ser Ser Ser Gly Pro Arg Lys His Leu Arg  
                   210                  215                  220  
 Thr Asp Ala Phe Ser Gln His His Leu Glu Pro Leu Glu Cys Pro Phe  
                   225                  230                  235                  240  
 Glu Arg Gln His Tyr Pro Glu Ala Tyr Ala Ser Pro Ser His Thr Lys  
                   245                  250                  255  
 Gly Glu Gln Glu Val Asn Thr Leu Ala Met Pro Met Ala Thr Pro Pro  
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&lt;210&gt; 253

&lt;211&gt; .2148

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 253

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&lt;210&gt; 254

&lt;211&gt; 509

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 254

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Met Glu Arg Arg Leu Trp Gly Ser Ile Gln Ser Arg Tyr Ile Ser
1          5          10          15
Met Ser Val Trp Thr Ser Pro Arg Arg Leu Val Glu Leu Ala Gly Gln
20          25          30
Ser Leu Leu Lys Asp Glu Ala Leu Ala Ile Ala Ala Leu Glu Leu Leu
35          40          45
Pro Arg Glu Leu Phe Pro Pro Leu Phe Met Ala Ala Phe Asp Gly Arg
50          55          60
His Ser Gln Thr Leu Lys Ala Met Val Gln Ala Trp Pro Phe Thr Cys
65          70          75          80
Leu Pro Leu Gly Val Leu Met Lys Gly Gln His Leu His Leu Glu Thr
85          90          95
Phe Lys Ala Val Leu Asp Gly Leu Asp Val Leu Leu Ala Gln Glu Val
100          105          110
Arg Pro Arg Arg Trp Lys Leu Gln Val Leu Asp Leu Arg Lys Asn Ser
115          120          125
His Gln Asp Phe Trp Thr Val Trp Ser Gly Asn Arg Ala Ser Leu Tyr
130          135          140
Ser Phe Pro Glu Pro Glu Ala Ala Gln Pro Met Thr Lys Lys Arg Lys
145          150          155          160
Val Asp Gly Leu Ser Thr Glu Ala Glu Gln Pro Phe Ile Pro Val Glu
165          170          175
Val Leu Val Asp Leu Phe Leu Lys Glu Gly Ala Cys Asp Glu Leu Phe
180          185          190
Ser Tyr Leu Ile Glu Lys Val Lys Arg Lys Lys Asn Val Leu Arg Leu
195          200          205
Cys Cys Lys Lys Leu Lys Ile Phe Ala Met Pro Met Gln Asp Ile Lys
210          215          220
Met Ile Leu Lys Met Val Gln Leu Asp Ser Ile Glu Asp Leu Glu Val
225          230          235          240
Thr Cys Thr Trp Lys Leu Pro Thr Leu Ala Lys Phe Ser Pro Tyr Leu
245          250          255
Gly Gln Met Ile Asn Leu Arg Arg Leu Leu Leu Ser His Ile His Ala
260          265          270
Ser Ser Tyr Ile Ser Pro Glu Lys Glu Glu Gln Tyr Ile Ala Gln Phe
275          280          285
Thr Ser Gln Phe Leu Ser Leu Gln Cys Leu Gln Ala Leu Tyr Val Asp
290          295          300
Ser Leu Phe Phe Leu Arg Gly Arg Leu Asp Gln Leu Leu Arg His Val
305          310          315          320
Met Asn Pro Leu Glu Thr Leu Ser Ile Thr Asn Cys Arg Leu Ser Glu

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Val	Leu	Ser	Leu	Ser	Gly	Val	Met	Leu	Thr	Asp	Val	Ser	Pro	Glu	Pro									
										355						360						365		
Leu	Gln	Ala	Leu	Leu	Glu	Arg	Ala	Ser	Ala	Thr	Leu	Gln	Asp	Leu	Val									
										370						375						380		
Phe	Asp	Glu	Cys	Gly	Ile	Thr	Asp	Asp	Gln	Leu	Leu	Ala	Leu	Leu	Pro									
										385						390						395		
Ser	Leu	Ser	His	Cys	Ser	Gln	Leu	Thr	Thr	Leu	Ser	Phe	Tyr	Gly	Asn									
										405						410						415		
Ser	Ile	Ser	Ile	Ser	Ala	Leu	Gln	Ser	Leu	Leu	Gln	His	Leu	Ile	Gly									
										420						425						430		
Leu	Ser	Asn	Leu	Thr	His	Val	Leu	Tyr	Pro	Val	Pro	Leu	Glu	Ser	Tyr									
										435						440						445		
Glu	Asp	Ile	His	Gly	Thr	Leu	His	Leu	Glu	Arg	Leu	Ala	Tyr	Leu	His									
										450						455						460		
Ala	Arg	Leu	Arg	Glu	Leu	Leu	Cys	Glu	Leu	Gly	Arg	Pro	Ser	Met	Val									
										465						470						475		
Trp	Leu	Ser	Ala	Asn	Pro	Cys	Pro	His	Cys	Gly	Asp	Arg	Thr	Phe	Tyr									
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Asp	Pro	Glu	Pro	Ile	Leu	Cys	Pro	Cys	Phe	Met	Pro	Asn												
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<210> 255
<211> 2261
<212> DNA
<213> Homo sapiens
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265

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&lt;210&gt; 256

&lt;211&gt; 587

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 256

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Glu Pro Ser Ile Ser Phe Glu Gly Leu Cys Asn Glu Val Arg Asp Met
 35          40          45
Cys Ser Phe Asp Asn Glu Gln Leu Phe Thr Met Lys Trp Ile Asp Glu
 50          55          60
Glu Gly Asp Pro Cys Thr Val Ser Ser Gln Leu Glu Leu Glu Ala
 65          70          75          80
Phe Arg Leu Tyr Glu Leu Asn Lys Asp Ser Glu Leu Leu Ile His Val
 85          90          95
Phe Pro Cys Val Pro Glu Arg Pro Gly Met Pro Cys Pro Gly Glu Asp
100          105          110
Lys Ser Ile Tyr Arg Arg Gly Ala Arg Arg Trp Arg Lys Leu Tyr Cys
115          120          125
Ala Asn Gly His Thr Phe Gln Ala Lys Arg Phe Asn Arg Arg Ala His
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Cys Ala Ile Cys Thr Asp Arg Ile Trp Gly Leu Gly Arg Gln Gly Tyr
145          150          155          160
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165          170          175
Val Thr Ile Glu Cys Gly Arg His Ser Leu Pro Gln Glu Pro Val Met
180          185          190
Pro Met Asp Gln Ser Ser Met His Ser Asp His Ala Gln Thr Val Ile
195          200          205
Pro Tyr Asn Pro Ser Ser His Glu Ser Leu Asp Gln Val Gly Glu Glu
210          215          220
Lys Glu Ala Met Asn Thr Arg Glu Ser Gly Lys Ala Ser Ser Ser Leu
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Gly Leu Gln Asp Phe Asp Leu Leu Arg Val Ile Gly Arg Gly Ser Tyr
245          250          255
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275          280          285
Trp Val Gln Thr Glu Lys His Val Phe Glu Gln Ala Ser Asn His Pro
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<211> 6742
<212> DNA
<213> Homo sapiens
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&lt;210&gt; 258

&lt;211&gt; 1043

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 258

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20           25           30
Arg Lys Phe Lys Met Ala Ala Ala Glu Thr Gln Ser Leu Arg Glu Gln
35           40           45
Pro Glu Met Glu Asp Ala Asn Ser Glu Lys Ser Ile Asn Glu Glu Asn
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Lys Lys Lys His Lys His Arg Ser Lys His Lys Lys His Lys His Ser
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Lys	Lys	Ser	Lys	Ser	Pro	Ser	Lys	Arg	Ser	Lys	Ser	Gln	Asp	Gln	Ala	260	265	270
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Gly	Lys	Ala	Arg	Ser	Pro	Thr	Asp	Asp	Lys	Val	Lys	Ile	Glu	Asp	Lys	290	295	300
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Asp	Ala	Ser	Pro	Ile	Asn	Arg	Trp	Ser	Pro	Thr	Arg	Arg	Arg	Ser	Arg	465	470	475
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Ser	Glu	Gly	Met	Lys	Val	Glu	Gln	Glu	Ser	Ser	Ser	Asp	Asp	Asn	Leu	545	550	555

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Asp	Ile	Thr	Pro	Tyr	Leu	Val	Ser	Arg	Phe	Tyr	Arg	Ala	Pro	Glu	Ile
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&lt;213&gt; Homo sapiens

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      85           90           95
Glu Val Lys Leu Gly Ala His Gln Leu Asp Ser Tyr Ser Glu Asp Ala
      100          105          110
Lys Val Ser Thr Leu Lys Asp Ile Ile Pro His Pro Ser Tyr Leu Gln
      115          120          125
Glu Gly Ser Gln Gly Asp Ile Ala Leu Leu Gln Leu Ser Arg Pro Ile
      130          135          140
Thr Phe Ser Arg Tyr Ile Arg Pro Ile Cys Leu Pro Ala Ala Asn Ala
      145          150          155          160
Ser Phe Pro Asn Gly Leu His Cys Thr Val Thr Gly Trp Gly His Val
      165          170          175
Ala Pro Ser Val Ser Leu Leu Thr Pro Lys Pro Leu Gln Gln Leu Glu
      180          185          190
Val Pro Leu Ile Ser Arg Glu Thr Cys Asn Cys Leu Tyr Asn Ile Asp
      195          200          205
Ala Lys Pro Glu Glu Pro His Phe Val Gln Glu Asp Met Val Cys Ala
      210          215          220
Gly Tyr Val Glu Gly Gly Lys Asp Ala Cys Gln Gly Asp Ser Gly Gly
      225          230          235          240
Pro Leu Ser Cys Pro Val Glu Gly Leu Trp Tyr Leu Thr Gly Ile Val
      245          250          255
Ser Trp Gly Asp Ala Cys Gly Ala Arg Asn Arg Pro Gly Val Tyr Thr
      260          265          270
Leu Ala Ser Ser Tyr Ala Ser Trp Ile Gln Ser Lys Val Thr Glu Leu
      275          280          285
Gln Pro Arg Val Val Pro Gln Thr Gln Glu Ser Gln Pro Asp Ser Asn
      290          295          300
Leu Cys Gly Ser His Leu Ala Phe Ser Ser Ala Pro Ala Gln Gly Leu
      305          310          315          320
Leu Arg Pro Ile Leu Phe Leu Pro Leu Gly Leu Ala Leu Gly Leu Leu
      325          330          335
Ser Pro Trp Leu Ser Glu His
      340

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&lt;210&gt; 263

&lt;211&gt; 2554

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 263

276

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&lt;210&gt; 264

&lt;211&gt; 599

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 264

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Pro Pro Leu Pro Val Leu Leu Ala Asp Pro Gly Ala Pro Thr Pro Val
      20             25            30
Asn Pro Cys Cys Tyr Tyr Pro Cys Gln His Gln Gly Ile Cys Val Arg
      35             40            45
Phe Gly Leu Asp Arg Tyr Gln Cys Asp Cys Thr Arg Thr Gly Tyr Ser
 50             55            60

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Gly	Pro	Asn	Cys	Thr	Ile	Pro	Gly	Leu	Trp	Thr	Trp	Leu	Arg	Asn	Ser
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Leu	Arg	Pro	Ser	Pro	Ser	Phe	Thr	His	Phe	Leu	Leu	Thr	His	Gly	Arg
				85					90					95	
Trp	Phe	Trp	Glu	Phe	Val	Asn	Ala	Thr	Phe	Ile	Arg	Glu	Met	Leu	Met
			100					105					110		
Arg	Leu	Val	Leu	Thr	Val	Arg	Ser	Asn	Leu	Ile	Pro	Ser	Pro	Pro	Thr
		115					120					125			
Tyr	Asn	Ser	Ala	His	Asp	Tyr	Ile	Ser	Trp	Glu	Ser	Phe	Ser	Asn	Val
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145					150					155					160
Pro	Met	Gly	Thr	Lys	Gly	Lys	Lys	Gln	Leu	Pro	Asp	Ala	Gln	Leu	Leu
				165					170					175	
Ala	Arg	Arg	Phe	Leu	Leu	Arg	Arg	Lys	Phe	Ile	Pro	Asp	Pro	Gln	Gly
			180					185					190		
Thr	Asn	Leu	Met	Phe	Ala	Phe	Phe	Ala	Gln	His	Phe	Thr	His	Gln	Phe
	195						200					205			
Phe	Lys	Thr	Ser	Gly	Lys	Met	Gly	Pro	Gly	Phe	Thr	Lys	Ala	Leu	Gly
210						215					220				
His	Gly	Val	Asp	Leu	Gly	His	Ile	Tyr	Gly	Asp	Asn	Leu	Glu	Arg	Gln
225					230					235					240
Tyr	Gln	Leu	Arg	Leu	Phe	Lys	Asp	Gly	Lys	Leu	Lys	Tyr	Gln	Val	Leu
				245					250					255	
Asp	Gly	Glu	Met	Tyr	Pro	Pro	Ser	Val	Glu	Glu	Ala	Pro	Val	Leu	Met
			260					265					270		
His	Tyr	Pro	Arg	Gly	Ile	Pro	Pro	Gln	Ser	Gln	Met	Ala	Val	Gly	Gln
	275					280						285			
Glu	Val	Phe	Gly	Leu	Leu	Pro	Gly	Leu	Met	Leu	Tyr	Ala	Thr	Leu	Trp
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Leu	Arg	Glu	His	Asn	Arg	Val	Cys	Asp	Leu	Leu	Lys	Ala	Glu	His	Pro
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Thr	Trp	Gly	Asp	Glu	Gln	Leu	Phe	Gln	Thr	Thr	Arg	Leu	Ile	Leu	Ile
				325					330					335	
Gly	Glu	Thr	Ile	Lys	Ile	Val	Ile	Glu	Glu	Tyr	Val	Gln	Gln	Leu	Ser
			340					345					350		
Gly	Tyr	Phe	Leu	Gln	Leu	Lys	Phe	Asp	Pro	Glu	Leu	Leu	Phe	Gly	Val
		355					360					365			
Gln	Phe	Gln	Tyr	Arg	Asn	Arg	Ile	Ala	Met	Glu	Phe	Asn	His	Leu	Tyr
	370					375					380				
His	Trp	His	Pro	Leu	Met	Pro	Asp	Ser	Phe	Lys	Val	Gly	Ser	Gln	Glu
385				390						395					400
Tyr	Ser	Tyr	Glu	Gln	Phe	Leu	Phe	Asn	Thr	Ser	Met	Leu	Val	Asp	Tyr
				405					410					415	
Gly	Val	Glu	Ala	Leu	Val	Asp	Ala	Phe	Ser	Arg	Gln	Ile	Ala	Gly	Arg
			420					425					430		
Ile	Gly	Gly	Gly	Arg	Asn	Met	Asp	His	His	Ile	Leu	His	Val	Ala	Val
		435					440					445			
Asp	Val	Ile	Arg	Glu	Ser	Arg	Glu	Met	Arg	Leu	Gln	Pro	Phe	Asn	Glu
	450					455					460				
Tyr	Arg	Lys	Arg	Phe	Gly	Met	Lys	Pro	Tyr	Thr	Ser	Phe	Gln	Glu	Leu
465					470					475					480
Val	Gly	Glu	Lys	Glu	Met	Ala	Ala	Glu	Leu	Glu	Glu	Leu	Tyr	Gly	Asp
				485					490					495	
Ile	Asp	Ala	Leu	Glu	Phe	Tyr	Pro	Gly	Leu	Leu	Leu	Glu	Lys	Cys	His
			500					505					510		
Pro	Asn	Ser	Ile	Phe	Gly	Glu	Ser	Met	Ile	Glu	Ile	Gly	Ala	Pro	Phe
		515					520					525			

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Ser Leu Lys Gly Leu Leu Gly Asn Pro Ile Cys Ser Pro Glu Tyr Trp  
 530 535 540  
 Lys Pro Ser Thr Phe Gly Gly Glu Val Gly Phe Asn Ile Val Lys Thr  
 545 550 555 560  
 Ala Thr Leu Lys Lys Leu Val Cys Leu Asn Thr Lys Thr Cys Pro Tyr  
 565 570 575  
 Val Ser Phe Arg Val Pro Asp Ala Ser Gln Asp Asp Gly Pro Ala Val  
 580 585 590  
 Glu Arg Pro Ser Thr Glu Leu  
 595

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 <211> 3000  
 <212> DNA  
 <213> Homo sapiens

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 tcatatagtc agccttcaga ttcttgggat aaggattatg attcctttgt tttacccttg 240  
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279

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&lt;210&gt; 266

&lt;211&gt; 350

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 266

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Phe Ala Arg Ala Arg Asn Gly Lys Tyr Arg Leu Leu Lys Ile Ser Ile
          20          25          30
Glu Asn Glu Gln Leu Val Ile Gly Ser Tyr Ser Gln Pro Ser Asp Ser
          35          40          45
Trp Asp Lys Asp Tyr Asp Ser Phe Val Leu Pro Leu Leu Glu Asp Lys
          50          55          60
Gln Pro Cys Tyr Ile Leu Phe Arg Leu Asp Ser Gln Asn Ala Gln Gly
65          70          75          80
Tyr Glu Trp Ile Phe Ile Ala Trp Ser Pro Asp His Ser His Val Arg
          85          90          95
Gln Lys Met Leu Tyr Ala Ala Thr Arg Ala Thr Leu Lys Lys Glu Phe
          100          105          110
Gly Gly Gly His Ile Lys Asp Glu Val Phe Gly Thr Val Lys Glu Asp
          115          120          125
Val Ser Leu His Gly Tyr Lys Lys Tyr Leu Leu Ser Gln Ser Ser Pro
          130          135          140
Ala Pro Leu Thr Ala Ala Glu Glu Glu Leu Arg Gln Ile Lys Ile Asn
145          150          155          160
Glu Val Gln Thr Asp Val Gly Val Asp Thr Lys His Gln Thr Leu Gln
          165          170          175
Gly Val Ala Phe Pro Ile Ser Arg Glu Ala Phe Gln Ala Leu Glu Lys
          180          185          190
Leu Asn Asn Arg Gln Leu Asn Tyr Val Gln Leu Glu Ile Asp Ile Lys
          195          200          205
Asn Glu Ile Ile Ile Leu Ala Asn Thr Thr Asn Thr Glu Leu Lys Asp
210          215          220
Leu Pro Lys Arg Ile Pro Lys Asp Ser Ala Arg Tyr His Phe Phe Leu
225          230          235          240
Tyr Lys His Ser His Glu Gly Asp Tyr Leu Glu Ser Ile Val Phe Ile
          245          250          255
Tyr Ser Met Pro Gly Tyr Thr Cys Ser Ile Arg Glu Arg Met Leu Tyr
          260          265          270
Ser Ser Cys Lys Ser Arg Leu Leu Glu Ile Val Glu Arg Gln Leu Gln
          275          280          285
Met Asp Val Ile Arg Lys Ile Glu Ile Asp Asn Gly Asp Glu Leu Thr
290          295          300
Ala Asp Phe Leu Tyr Glu Glu Val His Pro Lys Gln His Ala His Lys
305          310          315          320

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Arg Leu Ile Arg Gly Pro Ala Glu Thr Glu Ala Thr Thr Asp  
340 345 350

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cgaacacgcg	tgactacagc	glatggcggg	gtcgcggcac	tgtgcggctg	gacccccagt	240
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[illegible]

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atccctctcc	ataaccccac	ccttgcccac	cccaccccc	ccccaccaa	gggcgcaaga	540
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aaaaaaa						607

281

<210> 270  
 <211> 94  
 <212> PRT  
 <213> Homo sapiens

<400> 270  
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 20 25 30  
 Glu Leu Lys Glu Leu Leu Gln Thr Glu Leu Ser Gly Phe Leu Asp Ala  
 35 40 45  
 Gln Lys Asp Val Asp Ala Val Asp Lys Val Met Lys Glu Leu Asp Glu  
 50 55 60  
 Asn Gly Asp Gly Glu Val Asp Phe Gln Glu Tyr Val Val Leu Val Ala  
 65 70 75 80  
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 85 90

<210> 271  
 <211> 595  
 <212> DNA  
 <213> Homo sapiens

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 atggcaaaaa tctccagccc tacagagact gagcgggtgca tcgagtcctt gattgtgtc 180  
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 <211> 105  
 <212> PRT  
 <213> Homo sapiens

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 35 40 45  
 Ala Phe Thr Lys Asn Gln Lys Asp Pro Gly Val Leu Asp Arg Met Met  
 50 55 60  
 Lys Lys Leu Asp Thr Asn Ser Asp Gly Gln Leu Asp Phe Ser Glu Phe  
 65 70 75 80  
 Leu Asn Leu Ile Gly Gly Leu Ala Met Ala Cys His Asp Ser Phe Leu  
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 100 105

282

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 <211> 428  
 <212> DNA  
 <213> Homo sapiens

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 ggagaaagtg gatgaggagg ggctgaagaa gctgatgggc agcctggatg agaacagtga 240  
 ccagcaggtg gacttccagg agtatgctgt ttctctggca ctcatcactg tcatgtgcaa 300  
 tgacttcttc cagggctgcc cagaccgacc ctgaagcaga actcttgact tcctgccatg 360  
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 tctgttga 428

<210> 274  
 <211> 97  
 <212> PRT  
 <213> Homo sapiens

<400> 274  
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 1 5 10 15  
 His Lys Tyr Ser Cys Gln Glu Gly Asp Lys Phe Lys Leu Ser Lys Gly  
 20 25 30  
 Glu Met Lys Glu Leu Leu His Lys Glu Leu Pro Ser Phe Val Gly Glu  
 35 40 45  
 Lys Val Asp Glu Glu Gly Leu Lys Lys Leu Met Gly Ser Leu Asp Glu  
 50 55 60  
 Asn Ser Asp Gln Gln Val Asp Phe Gln Glu Tyr Ala Val Phe Leu Ala  
 65 70 75 80  
 Leu Ile Thr Val Met Cys Asn Asp Phe Phe Gln Gly Cys Pro Asp Arg  
 85 90 95  
 Pro

<210> 275  
 <211> 470  
 <212> DNA  
 <213> Homo sapiens

<400> 275  
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 catttgccg cctccctacc gctccaagcc cagccctcag ccatggcatg cccctggat 120  
 caggccattg gcctcctcgt ggccatcttc cacaagtact ccggcagga gggtgacaag 180  
 cacaccctga gcaagaagga gctgaaggag ctgatccaga aggagctcac cattggctcg 240  
 aagctgcagg atgctgaaat tgcaaggctg atggaagact tggaccgaa caaggaccag 300  
 gaggtgaact tccaggagta tgtcaccttc ctgggggcct tggctttgat ctacaatgaa 360  
 gccctcaagg gctgaaaata aatagggaag atggagacac ctctgggggt cctctctgag 420  
 tcaaatccag tgggtgggtaa ttgtacaata aatttttttt ggtcaaattt 470

<210> 276  
 <211> 90  
 <212> PRT  
 <213> Homo sapiens

283

&lt;400&gt; 276

Met Ala Cys Pro Leu Asp Gln Ala Ile Gly Leu Leu Val Ala Ile Phe  
 1 5 10 15  
 His Lys Tyr Ser Gly Arg Glu Gly Asp Lys His Thr Leu Ser Lys Lys  
 20 25 30  
 Glu Leu Lys Glu Leu Ile Gln Lys Glu Leu Thr Ile Gly Ser Lys Leu  
 35 40 45  
 Gln Asp Ala Glu Ile Ala Arg Leu Met Glu Asp Leu Asp Arg Asn Lys  
 50 55 60  
 Asp Gln Glu Val Asn Phe Gln Glu Tyr Val Thr Phe Leu Gly Ala Leu  
 65 70 75 80  
 Ala Leu Ile Tyr Asn Glu Ala Leu Lys Gly  
 85 90

&lt;210&gt; 277

&lt;211&gt; 3151

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 277

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 gagcaggact ctagccctcc acagtccact ccagggtctca tgaaggggaa caagcgtgag 180  
 gagcaggggc tgggccccga acctgcggcg cccagcagc ccacggcgga ggaggaggcc 240  
 ctgatcgagt tccaccgctc ctaccgagag ctcttcgagt tcttctgcaa caacaccacc 300  
 atccacggcg ccatccgcct ggtgtgctcc cagcacaacc gcatgaagac ggccttcttg 360  
 gcagtgtgtt ggctctgcac ctttggcatg atgtactggc aattcggcct gcttttctga 420  
 gagtacttca gctaccccggt cagcctcaac atcaacctca actcggacaa gctcgtcttc 480  
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 ttgcagcggt ttgaggtccc gccccgcct caccgggccc gtcgagccc tagcgtggag 720  
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 gggccctgag agggaaaggag aggtttctca caccaaggca gatgctcctc tgggtggagg 2160

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gtgctggccc tggcaagatt gaaggatgtg cagggcttcc tctcagagcc gcccaactg 2220
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caagcgaaac ttggagcttt gacaaggaac tttcctaaga aaccgctgat aaccaggaca 2460
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tctcccttcc caactagact gtaagtgcct tgcggtcagg gactgaatct tgcccgttta 3060
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tgtttgttgc atgaaaaaaa aaaaaaaaaa a 3151

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&lt;210&gt; 278

&lt;211&gt; 669

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 278

```

Met Glu Gly Asn Lys Leu Glu Glu Gln Asp Ser Ser Pro Pro Gln Ser
1      5      10      15
Thr Pro Gly Leu Met Lys Gly Asn Lys Arg Glu Glu Gln Gly Leu Gly
20      25      30
Pro Glu Pro Ala Ala Pro Gln Gln Pro Thr Ala Glu Glu Glu Ala Leu
35      40      45
Ile Glu Phe His Arg Ser Tyr Arg Glu Leu Phe Glu Phe Phe Cys Asn
50      55      60
Asn Thr Thr Ile His Gly Ala Ile Arg Leu Val Cys Ser Gln His Asn
65      70      75      80
Arg Met Lys Thr Ala Phe Trp Ala Val Leu Trp Leu Cys Thr Phe Gly
85      90      95
Met Met Tyr Trp Gln Phe Gly Leu Leu Phe Gly Glu Tyr Phe Ser Tyr
100     105     110
Pro Val Ser Leu Asn Ile Asn Leu Asn Ser Asp Lys Leu Val Phe Pro
115     120     125
Ala Val Thr Ile Cys Thr Leu Asn Pro Tyr Arg Tyr Pro Glu Ile Lys
130     135     140
Glu Glu Leu Glu Glu Leu Asp Arg Ile Thr Glu Gln Thr Leu Phe Asp
145     150     155     160
Leu Tyr Lys Tyr Ser Ser Phe Thr Thr Leu Val Ala Gly Ser Arg Ser
165     170     175
Arg Arg Asp Leu Arg Gly Thr Leu Pro His Pro Leu Gln Arg Leu Arg
180     185     190
Val Pro Pro Pro Pro His Gly Ala Arg Arg Ala Arg Ser Val Ala Ser
195     200     205
Ser Leu Arg Asp Asn Asn Pro Gln Val Asp Trp Lys Asp Trp Lys Ile
210     215     220
Gly Phe Gln Leu Cys Asn Gln Asn Lys Ser Asp Cys Phe Tyr Gln Thr
225     230     235     240
Tyr Ser Ser Gly Val Asp Ala Val Arg Glu Trp Tyr Arg Phe His Tyr
245     250     255
Ile Asn Ile Leu Ser Arg Leu Pro Glu Thr Leu Pro Ser Leu Glu Glu
260     265     270

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285

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Asp Thr Leu Gly Asn Phe Ile Phe Ala Cys Arg Phe Asn Gln Val Ser
      275      280      285
Cys Asn Gln Ala Asn Tyr Ser His Phe His His Pro Met Tyr Gly Asn
      290      295      300
Cys Tyr Thr Phe Asn Asp Lys Asn Asn Ser Asn Leu Trp Met Ser Ser
      305      310      315      320
Met Pro Gly Ile Asn Asn Gly Leu Ser Leu Met Leu Arg Ala Glu Gln
      325      330      335
Asn Asp Phe Ile Pro Leu Leu Ser Thr Val Thr Gly Ala Arg Val Met
      340      345      350
Val His Gly Gln Asp Glu Pro Ala Phe Met Asp Asp Gly Gly Phe Asn
      355      360      365
Leu Arg Pro Gly Val Glu Thr Ser Ile Ser Met Arg Lys Glu Thr Leu
      370      375      380
Asp Arg Leu Gly Gly Asp Tyr Gly Asp Cys Thr Lys Asn Gly Ser Asp
      385      390      395      400
Val Pro Val Glu Asn Leu Tyr Pro Ser Lys Tyr Thr Gln Gln Val Cys
      405      410      415
Ile His Ser Cys Phe Gln Glu Ser Met Ile Lys Glu Cys Gly Cys Ala
      420      425      430
Tyr Ile Phe Tyr Pro Arg Pro Gln Asn Val Glu Tyr Cys Asp Tyr Arg
      435      440      445
Lys His Ser Ser Trp Gly Tyr Cys Tyr Tyr Lys Leu Gln Val Asp Phe
      450      455      460
Ser Ser Asp His Leu Gly Cys Phe Thr Lys Cys Arg Lys Pro Cys Ser
      465      470      475      480
Val Thr Ser Tyr Gln Leu Ser Ala Gly Tyr Ser Arg Trp Pro Ser Val
      485      490      495
Thr Ser Gln Glu Trp Val Phe Gln Met Leu Ser Arg Gln Asn Asn Tyr
      500      505      510
Thr Val Asn Asn Lys Arg Asn Gly Val Ala Lys Val Asn Ile Phe Phe
      515      520      525
Lys Glu Leu Asn Tyr Lys Thr Asn Ser Glu Ser Pro Ser Val Thr Met
      530      535      540
Val Thr Leu Leu Ser Asn Leu Gly Ser Gln Trp Ser Leu Trp Phe Gly
      545      550      555      560
Ser Ser Val Leu Ser Val Val Glu Met Ala Glu Leu Val Phe Asp Leu
      565      570      575
Leu Val Ile Met Phe Leu Met Leu Leu Arg Arg Phe Arg Ser Arg Tyr
      580      585      590
Trp Ser Pro Gly Arg Gly Gly Arg Gly Ala Gln Glu Val Ala Ser Thr
      595      600      605
Leu Ala Ser Ser Pro Pro Ser His Phe Cys Pro His Pro Met Ser Leu
      610      615      620
Ser Leu Ser Gln Pro Gly Pro Ala Pro Ser Pro Ala Leu Thr Ala Pro
      625      630      635      640
Pro Pro Ala Tyr Ala Thr Leu Gly Pro Arg Pro Ser Pro Gly Gly Ser
      645      650      655
Ala Gly Ala Ser Ser Ser Thr Cys Pro Leu Gly Gly Pro
      660      665

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&lt;210&gt; 279

&lt;211&gt; 3174

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

<221> misc\_feature  
 <222> (1)... (3174)  
 <223> n = A, T, C or G

<400> 279

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tgctgtggct ctgcaccttt ggcatgatgt actggcaatt cggcctgctt ttccggagag 420
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cagtgacctat ctgcaccctc aatccctaca ggtaccgga aattaaagag gagctggagg 540
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&lt;210&gt; 280

&lt;211&gt; 669

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 280

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Met Glu Gly Asn Lys Leu Glu Glu Gln Asp Ser Ser Pro Pro Gln Ser
 1          5          10          15
Thr Pro Gly Leu Met Lys Gly Asn Lys Arg Glu Glu Gln Gly Leu Gly
      20          25          30
Pro Glu Pro Ala Ala Pro Gln Gln Pro Thr Ala Glu Glu Ala Leu
      35          40          45
Ile Glu Phe His Arg Ser Tyr Arg Glu Leu Phe Glu Phe Phe Cys Asn
      50          55          60
Asn Thr Thr Ile His Gly Ala Ile Arg Leu Val Cys Ser Gln His Asn
      65          70          75          80
Arg Met Lys Thr Ala Phe Trp Ala Val Leu Trp Leu Cys Thr Phe Gly
      85          90          95
Met Met Tyr Trp Gln Phe Gly Leu Leu Phe Gly Glu Tyr Phe Ser Tyr
      100          105          110
Pro Val Ser Leu Asn Ile Asn Leu Asn Ser Asp Lys Leu Val Phe Pro
      115          120          125
Ala Val Thr Ile Cys Thr Leu Asn Pro Tyr Arg Tyr Pro Glu Ile Lys
      130          135          140
Glu Glu Leu Glu Glu Leu Asp Arg Ile Thr Glu Gln Thr Leu Phe Asp
      145          150          155          160
Leu Tyr Lys Tyr Ser Ser Phe Thr Thr Leu Val Ala Gly Ser Arg Ser
      165          170          175
Arg Arg Asp Leu Arg Gly Thr Leu Pro His Pro Leu Gln Arg Leu Arg
      180          185          190
Val Pro Pro Pro Pro His Gly Ala Arg Arg Ala Arg Ser Val Ala Ser
      195          200          205
Ser Leu Arg Asp Asn Asn Pro Gln Val Asp Trp Lys Asp Trp Lys Ile
      210          215          220
Gly Phe Gln Leu Cys Asn Gln Asn Lys Ser Asp Cys Phe Tyr Gln Thr
      225          230          235          240
Tyr Ser Ser Gly Val Asp Ala Val Arg Glu Trp Tyr Arg Phe His Tyr
      245          250          255
Ile Asn Ile Leu Ser Arg Leu Pro Glu Thr Leu Pro Ser Leu Glu Glu
      260          265          270
Asp Thr Leu Gly Asn Phe Ile Phe Ala Cys Arg Phe Asn Gln Val Ser
      275          280          285
Cys Asn Gln Ala Asn Tyr Ser His Phe His His Pro Met Tyr Gly Asn
      290          295          300
Cys Tyr Thr Phe Asn Asp Lys Asn Asn Ser Asn Leu Trp Met Ser Ser
      305          310          315          320
Met Pro Gly Ile Asn Asn Gly Leu Ser Leu Met Leu Arg Ala Glu Gln
      325          330          335
Asn Asp Phe Ile Pro Leu Leu Ser Thr Val Thr Gly Ala Arg Val Met
      340          345          350
Val His Gly Gln Asp Glu Pro Ala Phe Met Asp Asp Gly Gly Phe Asn
      355          360          365
Leu Arg Pro Gly Val Glu Thr Ser Ile Ser Met Arg Lys Glu Thr Leu
      370          375          380
Asp Arg Leu Gly Gly Asp Tyr Gly Asp Cys Thr Lys Asn Gly Ser Asp
      385          390          395          400
Val Pro Val Glu Asn Leu Tyr Pro Ser Lys Tyr Thr Gln Gln Val Cys

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				405					410					415		
Ile	His	Ser	Cys	Phe	Gln	Glu	Ser	Met	Ile	Lys	Glu	Cys	Gly	Cys	Ala	
			420					425					430			
Tyr	Ile	Phe	Tyr	Pro	Arg	Pro	Gln	Asn	Val	Glu	Tyr	Cys	Asp	Tyr	Arg	
		435					440					445				
Lys	His	Ser	Ser	Trp	Gly	Tyr	Cys	Tyr	Tyr	Lys	Leu	Gln	Val	Asp	Phe	
	450					455					460					
Ser	Ser	Asp	His	Leu	Gly	Cys	Phe	Thr	Lys	Cys	Arg	Lys	Pro	Cys	Ser	
465				470					475					480		
Val	Thr	Ser	Tyr	Gln	Leu	Ser	Ala	Gly	Tyr	Ser	Arg	Trp	Pro	Ser	Val	
			485					490					495			
Thr	Ser	Gln	Glu	Trp	Val	Phe	Gln	Met	Leu	Ser	Arg	Gln	Asn	Asn	Tyr	
		500						505				510				
Thr	Val	Asn	Asn	Lys	Arg	Asn	Gly	Val	Ala	Lys	Val	Asn	Ile	Phe	Phe	
		515				520					525					
Lys	Glu	Leu	Asn	Tyr	Lys	Thr	Asn	Ser	Glu	Ser	Pro	Ser	Val	Thr	Met	
	530				535				540							
Val	Thr	Leu	Leu	Ser	Asn	Leu	Gly	Ser	Gln	Trp	Ser	Leu	Trp	Phe	Gly	
545				550					555					560		
Ser	Ser	Val	Leu	Ser	Val	Val	Glu	Met	Ala	Glu	Leu	Val	Phe	Asp	Leu	
			565					570					575			
Leu	Val	Ile	Met	Phe	Leu	Met	Leu	Leu	Arg	Arg	Phe	Arg	Ser	Arg	Tyr	
		580					585					590				
Trp	Ser	Pro	Gly	Arg	Gly	Gly	Arg	Gly	Ala	Gln	Glu	Val	Ala	Ser	Thr	
		595				600						605				
Leu	Ala	Ser	Ser	Pro	Pro	Ser	His	Phe	Cys	Pro	His	Pro	Met	Ser	Leu	
	610					615					620					
Ser	Leu	Ser	Gln	Pro	Gly	Pro	Ala	Pro	Ser	Pro	Ala	Leu	Thr	Ala	Pro	
625				630				635						640		
Pro	Pro	Ala	Tyr	Ala	Thr	Leu	Gly	Pro	Arg	Pro	Ser	Pro	Gly	Gly	Ser	
			645					650					655			
Ala	Gly	Ala	Ser	Ser	Ser	Ala	Cys	Pro	Leu	Gly	Gly	Pro				
		660					665									

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<210> 281
<211> 2892
<212> DNA
<213> Homo sapiens
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<400> 281						
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&lt;210&gt; 282

&lt;211&gt; 176

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 282

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Met Ser Ala Gly Gly Ala Ser Val Pro Pro Pro Pro Asn Pro Ala Val
  1          5          10          15
Ser Phe Pro Pro Pro Arg Val Thr Leu Pro Ala Gly Pro Asp Ile Leu
          20          25          30
Arg Thr Tyr Ser Gly Ala Phe Val Cys Leu Glu Ile Leu Phe Gly Gly
  35          40          45
Leu Val Trp Ile Leu Val Ala Ser Ser Asn Val Pro Leu Pro Leu Leu
  50          55          60
Gln Gly Trp Val Met Phe Val Ser Val Thr Ala Phe Phe Phe Ser Leu
  65          70          75          80
Leu Phe Leu Gly Met Phe Leu Ser Gly Met Val Ala Gln Ile Asp Ala
          85          90          95
Asn Trp Asn Phe Leu Asp Phe Ala Tyr His Phe Thr Val Phe Val Phe
          100          105          110
Tyr Phe Gly Ala Phe Leu Leu Glu Ala Ala Ala Thr Ser Leu His Asp
          115          120          125
Leu His Cys Asn Thr Thr Ile Thr Gly Gln Pro Leu Leu Ser Asp Asn
          130          135          140
Gln Tyr Asn Ile Asn Val Ala Ala Ser Ile Phe Ala Phe Met Thr Thr

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<400> 283						
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aataccaccg						2530

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<210> 284
<211> 771
<212> PRT
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&lt;213&gt; Homo sapiens

&lt;400&gt; 284

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Met Gly Trp Leu Thr Arg Ile Val Cys Leu Phe Trp Gly Val Leu Leu
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Thr Ala Arg Ala Asn Tyr Gln Asn Gly Lys Asn Asn Val Pro Arg Leu
          20          25          30
Lys Leu Ser Tyr Lys Glu Met Leu Glu Ser Asn Asn Val Ile Thr Phe
          35          40          45
Asn Gly Leu Ala Asn Ser Ser Tyr His Thr Phe Leu Leu Asp Glu
          50          55          60
Glu Arg Ser Arg Leu Tyr Val Gly Ala Lys Asp His Ile Phe Ser Phe
65          70          75          80
Asp Leu Val Asn Ile Lys Asp Phe Gln Lys Ile Val Trp Pro Val Ser
          85          90          95
Tyr Thr Arg Arg Asp Glu Cys Lys Trp Ala Gly Lys Asp Ile Leu Lys
          100          105          110
Glu Cys Ala Asn Phe Ile Lys Val Leu Lys Ala Tyr Asn Gln Thr His
          115          120          125
Leu Tyr Ala Cys Gly Thr Gly Ala Phe His Pro Ile Cys Thr Tyr Ile
130          135          140
Glu Ile Gly His His Pro Glu Asp Asn Ile Phe Lys Leu Glu Asn Ser
145          150          155          160
His Phe Glu Asn Gly Arg Gly Lys Ser Pro Tyr Asp Pro Lys Leu Leu
          165          170          175
Thr Ala Ser Leu Leu Ile Asp Gly Glu Leu Tyr Ser Gly Thr Ala Ala
          180          185          190
Asp Phe Met Gly Arg Asp Phe Ala Ile Phe Arg Thr Leu Gly His His
          195          200          205
His Pro Ile Arg Thr Glu Gln His Asp Ser Arg Trp Leu Asn Asp Pro
210          215          220
Lys Phe Ile Ser Ala His Leu Ile Ser Glu Ser Asp Asn Pro Glu Asp
225          230          235          240
Asp Lys Val Tyr Phe Phe Phe Arg Glu Asn Ala Ile Asp Gly Glu His
          245          250          255
Ser Gly Lys Ala Thr His Ala Arg Ile Gly Gln Ile Cys Lys Asn Asp
          260          265          270
Phe Gly Gly His Arg Ser Leu Val Asn Lys Trp Thr Thr Phe Leu Lys
          275          280          285
Ala Arg Leu Ile Cys Ser Val Pro Gly Pro Asn Gly Ile Asp Thr His
          290          295          300
Phe Asp Glu Leu Gln Asp Val Phe Leu Met Asn Phe Lys Asp Pro Lys
305          310          315          320
Asn Pro Val Val Tyr Gly Val Phe Thr Thr Ser Ser Asn Ile Phe Lys
          325          330          335
Gly Ser Ala Val Cys Met Tyr Ser Met Ser Asp Val Arg Arg Val Phe
          340          345          350
Leu Gly Pro Tyr Ala His Arg Asp Gly Pro Asn Tyr Gln Trp Val Pro
          355          360          365
Tyr Gln Gly Arg Val Pro Tyr Pro Arg Pro Gly Thr Cys Pro Ser Lys
          370          375          380
Thr Phe Gly Gly Phe Asp Ser Thr Lys Asp Leu Pro Asp Asp Val Ile
385          390          395          400
Thr Phe Ala Arg Ser His Pro Ala Met Tyr Asn Pro Val Phe Pro Met
          405          410          415
Asn Asn Arg Pro Ile Val Ile Lys Thr Asp Val Asn Tyr Gln Phe Thr
          420          425          430
Gln Ile Val Val Asp Arg Val Asp Ala Glu Asp Gly Gln Tyr Asp Val

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292

435	440	445
Met Phe Ile Gly Thr Asp Val Gly Thr Val Leu Lys Val Val Ser Ile		
450	455	460
Pro Lys Glu Thr Trp Tyr Asp Leu Glu Glu Val Leu Leu Glu Glu Met		
465	470	475
Thr Val Phe Arg Glu Pro Thr Ala Ile Ser Ala Met Glu Leu Ser Thr		
485	490	495
Lys Gln Gln Gln Leu Tyr Ile Gly Ser Thr Ala Gly Val Ala Gln Leu		
500	505	510
Pro Leu His Arg Cys Asp Ile Tyr Gly Lys Ala Cys Ala Glu Cys Cys		
515	520	525
Leu Ala Arg Asp Pro Tyr Cys Ala Trp Asp Gly Ser Ala Cys Ser Arg		
530	535	540
Tyr Phe Pro Thr Ala Lys Arg Arg Thr Arg Arg Gln Asp Ile Arg Asn		
545	550	555
Gly Asp Pro Leu Thr His Cys Ser Asp Leu His His Asp Asn His His		
565	570	575
Gly His Ser Pro Glu Glu Arg Ile Ile Tyr Gly Val Glu Asn Ser Ser		
580	585	590
Thr Phe Leu Glu Cys Ser Pro Lys Ser Gln Arg Ala Leu Val Tyr Trp		
595	600	605
Gln Phe Gln Arg Arg Asn Glu Glu Arg Lys Glu Glu Ile Arg Val Asp		
610	615	620
Asp His Ile Ile Arg Thr Asp Gln Gly Leu Leu Leu Arg Ser Leu Gln		
625	630	635
Gln Lys Asp Ser Gly Asn Tyr Leu Cys His Ala Val Glu His Gly Phe		
645	650	655
Ile Gln Thr Leu Leu Lys Val Thr Leu Glu Val Ile Asp Thr Glu His		
660	665	670
Leu Glu Glu Leu Leu His Lys Asp Asp Asp Gly Asp Gly Ser Lys Thr		
675	680	685
Lys Glu Met Ser Asn Ser Met Thr Pro Ser Gln Lys Val Trp Tyr Arg		
690	695	700
Asp Phe Met Gln Leu Ile Asn His Pro Asn Leu Asn Thr Met Asp Glu		
705	710	715
Phe Cys Glu Gln Val Trp Lys Arg Asp Arg Lys Gln Arg Arg Gln Arg		
725	730	735
Pro Gly His Thr Pro Gly Asn Ser Asn Lys Trp Lys His Leu Gln Glu		
740	745	750
Asn Lys Lys Gly Arg Asn Arg Arg Thr His Glu Phe Glu Arg Ala Pro		
755	760	765
Arg Ser Val		
770		

&lt;210&gt; 285

&lt;211&gt; 3041

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 285

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293

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aaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa a 3041

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&lt;210&gt; 286

&lt;211&gt; 418

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 286

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Met Pro Ser Ser Val Ser Trp Gly Ile Leu Leu Ala Gly Leu Cys
 1           5           10          15
Cys Leu Val Pro Val Ser Leu Ala Glu Asp Pro Gln Gly Asp Ala Ala
          20          25          30
Gln Lys Thr Asp Thr Ser His His Asp Gln Asp His Pro Thr Phe Asn
          35          40          45
Lys Ile Thr Pro Asn Leu Ala Glu Phe Ala Phe Ser Leu Tyr Arg Gln

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294

50	55	60
Leu Ala His Gln Ser	Asn Ser Thr Asn Ile Phe	Phe Ser Pro Val Ser
65	70	75
Ile Ala Thr Ala Phe	Ala Met Leu Ser Leu Gly Thr Lys	Ala Asp Thr
85	90	95
His Asp Glu Ile Leu	Glu Gly Leu Asn Phe Asn Leu Thr	Glu Ile Pro
100	105	110
Glu Ala Gln Ile His	Glu Gly Phe Gln Glu Leu Leu Arg Thr	Leu Asn
115	120	125
Gln Pro Asp Ser Gln	Leu Gln Leu Thr Thr Gly Asn Gly	Leu Phe Leu
130	135	140
Ser Glu Gly Leu Lys	Leu Val Asp Lys Phe Leu Glu Asp	Val Lys Lys
145	150	155
Leu Tyr His Ser Glu	Ala Phe Thr Val Asn Phe Gly Asp Thr	Glu Glu
165	170	175
Ala Lys Lys Gln Ile	Asn Asp Tyr Val Glu Lys Gly Thr	Gln Gly Lys
180	185	190
Ile Val Asp Leu Val	Lys Glu Leu Asp Arg Asp Thr Val	Phe Ala Leu
195	200	205
Val Asn Tyr Ile Phe	Phe Lys Gly Lys Trp Glu Arg Pro	Phe Glu Val
210	215	220
Lys Asp Thr Glu Glu	Glu Asp Phe His Val Asp Gln Val Thr	Thr Val
225	230	235
Lys Val Pro Met Met	Lys Arg Leu Gly Met Phe Asn Ile Gln	His Cys
245	250	255
Lys Lys Leu Ser Ser	Trp Val Leu Leu Met Lys Tyr Leu	Gly Asn Ala
260	265	270
Thr Ala Ile Phe Phe	Leu Pro Asp Glu Gly Lys Leu Gln	His Leu Glu
275	280	285
Asn Glu Leu Thr His	Asp Ile Ile Thr Lys Phe Leu Glu	Asn Glu Asp
290	295	300
Arg Arg Ser Ala Ser	Leu His Leu Pro Lys Leu Ser Ile Thr	Gly Thr
305	310	315
Tyr Asp Leu Lys Ser	Val Leu Gly Gln Leu Gly Ile Thr Lys	Val Phe
325	330	335
Ser Asn Gly Ala Asp	Leu Ser Gly Val Thr Glu Glu Ala Pro	Leu Lys
340	345	350
Leu Ser Lys Ala Val	His Lys Ala Val Leu Thr Ile Asp	Glu Lys Gly
355	360	365
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370	375	380
Pro Pro Glu Val Lys	Phe Asn Lys Pro Phe Val Phe Leu	Met Ile Glu
385	390	395
Gln Asn Thr Lys Ser	Pro Leu Phe Met Gly Lys Val Val	Asn Pro Thr
405	410	415
Gln Lys		

&lt;210&gt; 287

&lt;211&gt; 3928

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

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&lt;210&gt; 288

&lt;211&gt; 293

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 288

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Trp Asn Trp Ile Trp Arg Arg Cys Cys Arg Ala Ala Ser Ala Ala Val
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Leu Ala Pro Leu Gly Phe Thr Leu Arg Lys Pro Pro Ala Val Gly Arg
50     55     60
Asn Arg Arg His His Arg His Pro Arg Gly Gly Ser Cys Leu Ala Ala
65     70     75     80
Ala His His Arg Met Arg Trp Arg Ala Asp Gly Arg Ser Leu Glu Lys
85     90     95
Leu Pro Val His Met Gly Leu Val Ile Thr Glu Val Glu Gln Glu Pro
100    105    110
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115    120    125
Ile Ser Tyr Ile Ser Val Tyr Asp His Gln Gly Ile Phe Lys Arg Asn
130    135    140
Asn Ser Arg Leu Met Asp Glu Ile Leu Lys Gln Gln Gln Glu Leu Leu
145    150    155    160
Gly Leu Asp Cys Ser Lys Tyr Ser Pro Glu Phe Ala Asn Ser Asn Asp
165    170    175
Lys Asp Asp Gln Val Leu Asn Cys His Leu Ala Val Lys Val Leu Ser
180    185    190
Pro Glu Asp Gly Lys Ala Asp Ile Val Arg Ala Ala Gln Asp Phe Cys
195    200    205
Gln Leu Val Ala Gln Lys Gln Lys Arg Pro Thr Asp Leu Asp Val Asp
210    215    220
Thr Leu Ala Ser Leu Leu Ser Ser Asn Gly Cys Pro Asp Pro Asp Leu
225    230    235    240
Val Leu Lys Phe Gly Pro Val Asp Ser Thr Leu Gly Phe Leu Pro Trp
245    250    255
His Ile Arg Leu Thr Glu Ile Val Ser Leu Pro Ser His Leu Asn Ile
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Gln Arg Leu Gly Lys
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&lt;210&gt; 289

297

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 <212> PRT  
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 Gly Val Glu Lys Leu Val Leu Ser Lys Leu Tyr Glu Glu Gly Ser Asn  
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 Lys Arg Leu Phe Asn Val Asp Arg His Val Gly Met Ala Val Ala Gly  
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 <212> PRT  
 <213> Homo sapiens

<400> 292

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Ser	Val	Arg	Arg	His	Met	Ile	Lys	His	Thr	Gly	Asn	Gly	Pro	Tyr	Lys
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Cys	Lys	Val	Cys	Gly	Lys	Ala	Phe	Asp	Phe	Pro	Ser	Ser	Phe	Arg	Ile
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His	Glu	Arg	Thr	His	Thr	Gly	Glu	Lys	Pro	Tyr	Asp	Cys	Lys	Gln	Cys
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Gly	Lys	Ala	Phe	Ser	Cys	Ser	Ser	Ser	Phe	Arg	Lys	His	Glu	Arg	Ile
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300

Lys Pro Tyr Glu Cys Lys Gln Cys Gly Lys Ala Phe Ser Arg Ser Thr  
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 Tyr Phe Arg Val His Glu Lys Ile His Thr Gly Glu Lys Pro Tyr Glu  
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<210> 293  
 <211> 666  
 <212> DNA  
 <213> Homo sapiens

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<210> 294  
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<400> 294  
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 <212> DNA  
 <213> Homo sapiens

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 ctgccatatg gaggaggctc tggagtctgt ctctgtgtgg tccaggctct ttccaccctg 480  
 agacttggtc ccaccactga tatctctctt tggggaaagg cttggcacac agcaggcttt 540

301

caagaagtgc cagttgatca atgaataaat aaacgagcct atttctcttt gcac 594

<210> 296

<211> 132

<212> PRT

<213> Homo sapiens

<400> 296

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Met Lys Ser Ser Gly Leu Phe Pro Phe Leu Val Leu Leu Ala Leu Gly
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      20           25           30
Gly Val Cys Pro Pro Lys Lys Ser Ala Gln Cys Leu Arg Tyr Lys Lys
      35           40           45
Pro Glu Cys Gln Ser Asp Trp Gln Cys Pro Gly Lys Lys Arg Cys Cys
      50           55           60
Pro Asp Thr Cys Gly Ile Lys Cys Leu Asp Pro Val Asp Thr Pro Asn
65           70           75           80
Pro Thr Arg Arg Lys Pro Gly Lys Cys Pro Val Thr Tyr Gly Gln Cys
      85           90           95
Leu Met Leu Asn Pro Pro Asn Phe Cys Glu Met Asp Gly Gln Cys Lys
      100          105          110
Arg Asp Leu Lys Cys Cys Met Gly Met Cys Gly Lys Ser Cys Val Ser
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Pro Val Lys Ala
      130

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<210> 297

<211> 720

<212> DNA

<213> Homo sapiens

<400> 297

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<210> 298

<211> 127

<212> PRT

<213> Homo sapiens

<400> 298

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Gly Ala Val Glu Lys Thr Lys Gln Gly Val Thr Glu Ala Ala Glu Lys
      20           25           30

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302

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Val	Gln	Ser	Val	Thr	Ser	Val	Ala	Glu	Lys	Thr	Lys	Glu	Gln	Ala	Asn
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Ala	Val	Ser	Glu	Ala	Val	Ser	Ser	Val	Asn	Thr	Val	Ala	Thr	Lys	
65					70				75					80	
Thr	Val	Glu	Glu	Ala	Glu	Asn	Ile	Ala	Val	Thr	Ser	Gly	Val	Val	Arg
				85				90						95	
Lys	Glu	Asp	Leu	Arg	Pro	Ser	Ala	Pro	Gln	Gln	Glu	Gly	Val	Ala	Ser
			100					105					110		
Lys	Glu	Lys	Glu	Glu	Val	Ala	Glu	Glu	Ala	Gln	Ser	Gly	Gly	Asp	
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&lt;210&gt; 299

&lt;211&gt; 6981

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 299

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304

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&lt;210&gt; 300

&lt;211&gt; 2214

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 300

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20 25 30
Gln Arg Leu His Gly Gly Ser Ala Pro Leu Pro Gln Asp Arg Gly Phe
35 40 45
Leu Val Val Gln Gly Asp Pro Arg Glu Leu Arg Leu Trp Ala Arg Gly
50 55 60
Asp Ala Arg Gly Ala Ser Arg Ala Asp Glu Lys Pro Leu Arg Arg Lys
65 70 75 80
Arg Ser Ala Ala Leu Gln Pro Glu Pro Ile Lys Val Tyr Gly Gln Val
85 90 95
Ser Leu Asn Asp Ser His Asn Gln Met Val Val His Trp Ala Gly Glu
100 105 110
Lys Ser Asn Val Ile Val Ala Leu Ala Arg Asp Ser Leu Ala Leu Ala
115 120 125
Arg Pro Lys Ser Ser Asp Val Tyr Val Ser Tyr Asp Tyr Gly Lys Ser
130 135 140
Phe Lys Lys Ile Ser Asp Lys Leu Asn Phe Gly Leu Gly Asn Arg Ser
145 150 155 160
Glu Ala Val Ile Ala Gln Phe Tyr His Ser Pro Ala Asp Asn Lys Arg
165 170 175
Tyr Ile Phe Ala Asp Ala Tyr Ala Gln Tyr Leu Trp Ile Thr Phe Asp
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Phe Cys Asn Thr Leu Gln Gly Phe Ser Ile Pro Phe Arg Ala Ala Asp
195 200 205
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210 215 220
Ser His Pro Asn Lys Gln Leu Trp Lys Ser Asp Asp Phe Gly Gln Thr
225 230 235 240

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305

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 275 280 285  
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 290 295 300  
 Lys Tyr Met Phe Ala Thr Lys Val Val His Leu Leu Gly Ser Glu Gln  
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 340 345 350  
 Asp Ala Ser Glu Asp Gln Val Phe Val Cys Val Ser His Ser Asn Asn  
 355 360 365  
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 385 390 395 400  
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 405 410 415  
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 420 425 430  
 Met Asn Glu Glu Asn Met Arg Ser Val Ile Thr Phe Asp Lys Gly Gly  
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 485 490 495  
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 500 505 510  
 Asn Leu Ala Ser Lys Thr Asn Val Tyr Ile Ser Ser Ser Ala Gly Ala  
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 545 550 555 560  
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 580 585 590  
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 610 615 620  
 Cys Thr Glu Asn Asp Tyr Lys Leu Trp Ser Pro Ser Asp Glu Arg Gly  
 625 630 635 640  
 Asn Glu Cys Leu Leu Gly His Lys Thr Val Phe Lys Arg Arg Thr Pro  
 645 650 655  
 His Ala Thr Cys Phe Asn Gly Glu Asp Phe Asp Arg Pro Val Val Val  
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 Lys Met Ser Glu Asp Leu Ser Leu Glu Val Cys Val Pro Asp Pro Glu  
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306

Phe	Ser	Gly	Lys	Ser	Tyr	Ser	Pro	Pro	Val	Pro	Cys	Pro	Val	Gly	Ser	705	710	715	720
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Pro	Leu	Ala	Glu	Glu	Asn	Glu	Phe	Ile	Leu	Tyr	Ala	Val	Arg	Lys	Ser	755	760	765	
Ile	Tyr	Arg	Tyr	Asp	Leu	Ala	Ser	Gly	Ala	Thr	Glu	Gln	Leu	Pro	Leu	770	775	780	
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Cys	Leu	Tyr	Trp	Ser	Asp	Leu	Ala	Leu	Asp	Val	Ile	Gln	Arg	Leu	Cys	805	810	815	
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Thr	Val	Glu	Ala	Leu	Ala	Phe	Glu	Pro	Leu	Ser	Gln	Leu	Leu	Tyr	Trp	835	840	845	
Val	Asp	Ala	Gly	Phe	Lys	Lys	Ile	Glu	Val	Ala	Asn	Pro	Asp	Gly	Asp	850	855	860	
Phe	Arg	Leu	Thr	Ile	Val	Asn	Ser	Ser	Val	Leu	Asp	Arg	Pro	Arg	Ala	865	870	875	880
Leu	Val	Leu	Val	Pro	Gln	Glu	Gly	Val	Met	Phe	Trp	Thr	Asp	Trp	Gly	885	890	895	
Asp	Leu	Lys	Pro	Gly	Ile	Tyr	Arg	Ser	Asn	Met	Asp	Gly	Ser	Ala	Ala	900	905	910	
Tyr	His	Leu	Val	Ser	Glu	Asp	Val	Lys	Trp	Pro	Asn	Gly	Ile	Ser	Val	915	920	925	
Asp	Asp	Gln	Trp	Ile	Tyr	Trp	Thr	Asp	Ala	Tyr	Leu	Glu	Cys	Ile	Glu	930	935	940	
Arg	Ile	Thr	Phe	Ser	Gly	Gln	Gln	Arg	Ser	Val	Ile	Leu	Asp	Asn	Leu	945	950	955	960
Pro	His	Pro	Tyr	Ala	Ile	Ala	Val	Phe	Lys	Asn	Glu	Ile	Tyr	Trp	Asp	965	970	975	
Asp	Trp	Ser	Gln	Leu	Ser	Ile	Phe	Arg	Ala	Ser	Lys	Tyr	Ser	Gly	Ser	980	985	990	
Gln	Met	Glu	Ile	Leu	Ala	Asn	Gln	Leu	Thr	Gly	Leu	Met	Asp	Met	Lys	995	1000	1005	
Ile	Phe	Tyr	Lys	Gly	Lys	Asn	Thr	Gly	Ser	Asn	Ala	Cys	Val	Pro	Arg	1010	1015	1020	
Pro	Cys	Ser	Leu	Leu	Cys	Leu	Pro	Lys	Ala	Asn	Asn	Ser	Arg	Ser	Cys	1025	1030	1035	1040
Arg	Cys	Pro	Glu	Asp	Val	Ser	Ser	Ser	Val	Leu	Pro	Ser	Gly	Asp	Leu	1045	1050	1055	
Met	Cys	Asp	Cys	Pro	Gln	Gly	Tyr	Gln	Leu	Lys	Asn	Asn	Thr	Cys	Val	1060	1065	1070	
Lys	Glu	Glu	Asn	Thr	Cys	Leu	Arg	Asn	Gln	Tyr	Arg	Cys	Ser	Asn	Gly	1075	1080	1085	
Asn	Cys	Ile	Asn	Ser	Ile	Trp	Trp	Cys	Asp	Phe	Asp	Asn	Asp	Cys	Gly	1090	1095	1100	
Asp	Met	Ser	Asp	Glu	Arg	Asn	Cys	Pro	Thr	Thr	Ile	Cys	Asp	Leu	Asp	1105	1110	1115	1120
Thr	Gln	Phe	Arg	Cys	Gln	Glu	Ser	Gly	Thr	Cys	Ile	Pro	Leu	Ser	Tyr	1125	1130	1135	
Lys	Cys	Asp	Leu	Glu	Asp	Asp	Cys	Gly	Asp	Asn	Ser	Asp	Glu	Ser	His	1140	1145	1150	
Cys	Glu	Met	His	Gln	Cys	Arg	Ser	Asp	Glu	Tyr	Asn	Cys	Ser	Ser	Gly	1155	1160	1165	

307

Met Cys Ile Arg Ser Ser Trp Val Cys Asp Gly Asp Asn Asp Cys Arg  
 1170 1175 1180  
 Asp Trp Ser Asp Glu Ala Asn Cys Thr Ala Ile Tyr His Thr Cys Glu  
 1185 1190 1195 1200  
 Ala Ser Asn Phe Gln Cys Arg Asn Gly His Cys Ile Pro Gln Arg Trp  
 1205 1210 1215  
 Ala Cys Asp Gly Asp Thr Asp Cys Gln Asp Gly Ser Asp Glu Asp Pro  
 1220 1225 1230  
 Val Asn Cys Glu Lys Lys Cys Asn Gly Phe Arg Cys Pro Asn Gly Thr  
 1235 1240 1245  
 Cys Ile Pro Ser Ser Lys His Cys Asp Gly Leu Arg Asp Cys Ser Asp  
 1250 1255 1260  
 Gly Ser Asp Glu Gln His Cys Glu Pro Leu Cys Thr His Phe Met Asp  
 1265 1270 1275 1280  
 Phe Val Cys Lys Asn Arg Gln Gln Cys Leu Phe His Ser Met Val Cys  
 1285 1290 1295  
 Asp Gly Ile Ile Gln Cys Arg Asp Gly Ser Asp Glu Asp Ala Ala Phe  
 1300 1305 1310  
 Ala Gly Cys Ser Gln Asp Pro Glu Phe His Lys Val Cys Asp Glu Phe  
 1315 1320 1325  
 Gly Phe Gln Cys Gln Asn Gly Val Cys Ile Ser Leu Ile Trp Lys Cys  
 1330 1335 1340  
 Asp Gly Met Asp Asp Cys Gly Asp Tyr Ser Asp Glu Ala Asn Cys Glu  
 1345 1350 1355 1360  
 Asn Pro Thr Glu Ala Pro Asn Cys Ser Arg Tyr Phe Gln Phe Arg Cys  
 1365 1370 1375  
 Glu Asn Gly His Cys Ile Pro Asn Arg Trp Lys Cys Asp Arg Glu Asn  
 1380 1385 1390  
 Asp Cys Gly Asp Trp Ser Asp Glu Lys Asp Cys Gly Asp Ser His Ile  
 1395 1400 1405  
 Leu Pro Phe Ser Thr Pro Gly Pro Ser Thr Cys Leu Pro Asn Tyr Tyr  
 1410 1415 1420  
 Arg Cys Ser Ser Gly Thr Cys Val Met Asp Thr Trp Val Cys Asp Gly  
 1425 1430 1435 1440  
 Tyr Arg Asp Cys Ala Asp Gly Ser Asp Glu Glu Ala Cys Pro Leu Leu  
 1445 1450 1455  
 Ala Asn Val Thr Ala Ala Ser Thr Pro Thr Gln Leu Gly Arg Cys Asp  
 1460 1465 1470  
 Arg Phe Glu Phe Glu Cys His Gln Pro Lys Thr Cys Ile Pro Asn Trp  
 1475 1480 1485  
 Lys Arg Cys Asp Gly His Gln Asp Cys Gln Asp Gly Arg Asp Glu Ala  
 1490 1495 1500  
 Asn Cys Pro Thr His Ser Thr Leu Thr Cys Met Ser Arg Glu Phe Gln  
 1505 1510 1515 1520  
 Cys Glu Asp Gly Glu Ala Cys Ile Val Leu Ser Glu Arg Cys Asp Gly  
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 Phe Leu Asp Cys Ser Asp Glu Ser Asp Glu Lys Ala Cys Ser Asp Glu  
 1540 1545 1550  
 Leu Thr Val Tyr Lys Val Gln Asn Leu Gln Trp Thr Ala Asp Phe Ser  
 1555 1560 1565  
 Gly Asp Val Thr Leu Thr Trp Met Arg Pro Lys Lys Met Pro Ser Ala  
 1570 1575 1580  
 Ser Cys Val Tyr Asn Val Tyr Tyr Arg Val Val Gly Glu Ser Ile Trp  
 1585 1590 1595 1600  
 Lys Thr Leu Glu Thr His Ser Asn Lys Thr Asn Thr Val Leu Lys Val  
 1605 1610 1615  
 Leu Lys Pro Asp Thr Thr Tyr Gln Val Lys Val Gln Val Gln Cys Leu  
 1620 1625 1630

308

Ser Lys Ala His Asn Thr Asn Asp Phe Val Thr Leu Arg Thr Pro Glu  
 1635 1640 1645  
 Gly Leu Pro Asp Ala Pro Arg Asn Leu Gln Leu Ser Leu Pro Arg Glu  
 1650 1655 1660  
 Ala Glu Gly Val Ile Val Gly His Trp Ala Pro Pro Ile His Thr His  
 1665 1670 1675 1680  
 Gly Leu Ile Arg Glu Tyr Ile Val Glu Tyr Ser Arg Ser Gly Ser Lys  
 1685 1690 1695  
 Met Trp Ala Ser Gln Arg Ala Ala Ser Asn Phe Thr Glu Ile Lys Asn  
 1700 1705 1710  
 Leu Leu Val Asn Thr Leu Tyr Thr Val Arg Val Ala Ala Val Thr Ser  
 1715 1720 1725  
 Arg Gly Ile Gly Asn Trp Ser Asp Ser Lys Ser Ile Thr Thr Ile Lys  
 1730 1735 1740  
 Gly Lys Val Ile Pro Pro Pro Asp Ile His Ile Asp Ser Tyr Gly Glu  
 1745 1750 1755 1760  
 Asn Tyr Leu Ser Phe Thr Leu Thr Met Glu Ser Asp Ile Lys Val Asn  
 1765 1770 1775  
 Gly Tyr Val Val Asn Leu Phe Trp Ala Phe Asp Thr His Lys Gln Glu  
 1780 1785 1790  
 Arg Arg Thr Leu Asn Phe Arg Gly Ser Ile Leu Ser His Lys Val Gly  
 1795 1800 1805  
 Asn Leu Thr Ala His Thr Ser Tyr Glu Ile Ser Ala Trp Ala Lys Thr  
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 Asp Leu Gly Asp Ser Pro Leu Ala Phe Glu His Val Met Thr Arg Gly  
 1825 1830 1835 1840  
 Val Arg Pro Pro Ala Pro Ser Leu Lys Ala Lys Ala Ile Asn Gln Thr  
 1845 1850 1855  
 Ala Val Glu Cys Thr Trp Thr Gly Pro Arg Asn Val Val Tyr Gly Ile  
 1860 1865 1870  
 Phe Tyr Ala Thr Ser Phe Leu Asp Leu Tyr Arg Asn Pro Lys Ser Leu  
 1875 1880 1885  
 Thr Thr Ser Leu His Asn Lys Thr Val Ile Val Ser Lys Asp Glu Gln  
 1890 1895 1900  
 Tyr Leu Phe Leu Val Arg Val Val Val Pro Tyr Gln Gly Pro Ser Ser  
 1905 1910 1915 1920  
 Asp Tyr Val Val Val Lys Met Ile Pro Asp Ser Arg Leu Pro Pro Arg  
 1925 1930 1935  
 His Leu His Val Val His Thr Gly Lys Thr Ser Val Val Ile Lys Trp  
 1940 1945 1950  
 Glu Ser Pro Tyr Asp Ser Pro Asp Gln Asp Leu Leu Tyr Ala Ile Ala  
 1955 1960 1965  
 Val Lys Asp Leu Ile Arg Lys Thr Asp Arg Ser Tyr Lys Val Lys Ser  
 1970 1975 1980  
 Arg Asn Ser Thr Val Glu Tyr Thr Leu Asn Lys Leu Glu Pro Gly Gly  
 1985 1990 1995 2000  
 Lys Tyr His Ile Ile Val Gln Leu Gly Asn Met Ser Lys Asp Ser Ser  
 2005 2010 2015  
 Ile Lys Ile Thr Thr Val Ser Leu Ser Ala Pro Asp Ala Leu Lys Ile  
 2020 2025 2030  
 Ile Thr Glu Asn Asp His Val Leu Leu Phe Trp Lys Ser Leu Ala Leu  
 2035 2040 2045  
 Lys Glu Lys His Phe Asn Glu Ser Arg Gly Tyr Glu Ile His Met Phe  
 2050 2055 2060  
 Asp Ser Ala Met Asn Ile Thr Ala Tyr Leu Gly Asn Thr Thr Asp Asn  
 2065 2070 2075 2080  
 Phe Phe Lys Ile Ser Asn Leu Lys Met Gly His Asn Tyr Thr Phe Thr  
 2085 2090 2095

309

Val Gln Ala Arg Cys Leu Phe Gly Asn Gln Ile Cys Gly Glu Pro Ala  
 2100 2105 2110  
 Ile Leu Leu Tyr Asp Glu Leu Gly Ser Gly Ala Asp Ala Ser Ala Thr  
 2115 2120 2125  
 Gln Ala Ala Arg Ser Thr Asp Val Ala Ala Val Val Val Pro Ile Leu  
 2130 2135 2140  
 Phe Leu Ile Leu Leu Ser Leu Gly Val Gly Phe Ala Ile Leu Tyr Thr  
 2145 2150 2155 2160  
 Lys His Arg Arg Leu Gln Ser Ser Phe Thr Ala Phe Ala Asn Ser His  
 2165 2170 2175  
 Tyr Ser Ser Arg Leu Gly Ser Ala Ile Phe Ser Ser Gly Asp Asp Leu  
 2180 2185 2190  
 Gly Glu Asp Asp Glu Asp Ala Pro Met Ile Thr Gly Phe Ser Asp Asp  
 2195 2200 2205  
 Val Pro Met Val Ile Ala  
 2210

<210> 301  
 <211> 1544  
 <212> DNA  
 <213> Homo sapiens

<220>  
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 ccacactgaa ggtccggaaa ggcgacttcc gggggctttg gcacctggcg gacctcccgc 180  
 gagcgtcggc acctgaacgc gaggcgctcc attgcgcgtg cgcgttgagg ggcttcccgc 240  
 acctgatcgc gagaccccaa cggctggtgg cgtcgcctgc gcgtctcggc tgagctggcc 300  
 atggcgcagc tgtgcgggct gaggcggagc cgggcgtttc tcgccctgct gggatcgtctg 360  
 ctctctctctg gggctctggc ggccgaccga gaacgcagca tccacgactt ctgcctgggtg 420  
 tcgaagggtg tgggcagatg ccgggcctcc atgcctagggt ggtggtacaa tgtcactgac 480  
 ggatcctgcc agctgtttgt gtatgggggc tgtgacggaa acagcaataa ttacctgacc 540  
 aaggaggagt gcctcaagaa atgtgccact gtcacagaga atgccacggg tgacctggcc 600  
 accagcagga atgcagcgga ttcctctgtc ccaagtgtc ccagaaggca ggattctgaa 660  
 gacctatcca gcgatatgtt caactatgaa gaatactgca ccgccaacgc agtactggg 720  
 ccttgccgtg catccttccc acgctggtac tttgacgtgg agaggaaactc ctgcaataac 780  
 ttcatctatg gaggtgccc gggcaataag aacagctacc gctctgagga ggcctgcatg 840  
 ctccgctgct tccgccagca ggagaatcct cccctgcccc ttggctcaa ggtggtggtt 900  
 ctggcggggc tgttcgtgat ggtgttgatc ctcttctctg gagectccat ggtctacctg 960  
 atccgggtg caggaggaa ccaggagcgt gccctgcgca ccgtctggag ctccggagat 1020  
 gacaaggagc agctggtgaa gaacacatat gtcctgtgac cgccctgtcg ccaagaggac 1080  
 tggggaaggg aggggagact atgtgtgagc tttttttaa tagagggatt gactcggatt 1140  
 tgagtgatca ttagggctga ggtctgtttc tctgggaggt aggacggctg cttcctggtc 1200  
 tggcagggat gggtttgctt tggaaatcct ctaggaggct cctcctcgca tggcctgcag 1260  
 tctggcagca gccccgagtt gtttcctcgc tgatcgattt ctttctcca ggtagagttt 1320  
 tctttgctta tgttgaaatc cattgcctcc ttttctcnat cacagaagtg atgttggaat 1380  
 cgtttctttt gtttgtctga tttatggttt ttttaagtat aaacaaaagt tttttattag 1440  
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 aataaatttc cagcatgttg ctttcaaaaa aaaaaaaaaa aaaa 1544

<210> 302  
 <211> 252

310

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 302

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          20           25           30
Ser Ile His Asp Phe Cys Leu Val Ser Lys Val Val Gly Arg Cys Arg
          35           40           45
Ala Ser Met Pro Arg Trp Trp Tyr Asn Val Thr Asp Gly Ser Cys Gln
 50           55           60
Leu Phe Val Tyr Gly Gly Cys Asp Gly Asn Ser Asn Asn Tyr Leu Thr
 65           70           75           80
Lys Glu Glu Cys Leu Lys Lys Cys Ala Thr Val Thr Glu Asn Ala Thr
          85           90           95
Gly Asp Leu Ala Thr Ser Arg Asn Ala Ala Asp Ser Ser Val Pro Ser
          100          105          110
Ala Pro Arg Arg Gln Asp Ser Glu Asp His Ser Ser Asp Met Phe Asn
          115          120          125
Tyr Glu Glu Tyr Cys Thr Ala Asn Ala Val Thr Gly Pro Cys Arg Ala
          130          135          140
Ser Phe Pro Arg Trp Tyr Phe Asp Val Glu Arg Asn Ser Cys Asn Asn
          145          150          155          160
Phe Ile Tyr Gly Gly Cys Arg Gly Asn Lys Asn Ser Tyr Arg Ser Glu
          165          170          175
Glu Ala Cys Met Leu Arg Cys Phe Arg Gln Gln Glu Asn Pro Pro Leu
          180          185          190
Pro Leu Gly Ser Lys Val Val Val Leu Ala Gly Leu Phe Val Met Val
          195          200          205
Leu Ile Leu Phe Leu Gly Ala Ser Met Val Tyr Leu Ile Arg Val Ala
          210          215          220
Arg Arg Asn Gln Glu Arg Ala Leu Arg Thr Val Trp Ser Ser Gly Asp
          225          230          235          240
Asp Lys Glu Gln Leu Val Lys Asn Thr Tyr Val Leu
          245          250

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&lt;210&gt; 303

&lt;211&gt; 1558

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(1558)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 303

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gaacgcgctg agggccgttg agtgtcgag gcggcgaggg cgcgagtgag gagcagaccc 120
aggcatcgcg cgccgagaag gccgggcgtc cccacactga aggtccgga aggcgacttc 180
cgggggcttt ggcacctggc ggacctccc ggagcgtcgg cacctgaacg cgaggcgtc 240
cattgcgcgt gcgcgttgag gggttcccg cacctgatcg cgagacccca acggctggtg 300
cgctcgctg cgctctcgg ctgagctggc catggcgag ctgtgcgggc tgaggcggag 360
ccgggcgttt ctgcacctgc tgggatcgct gctcctctct ggggtcctgg cgccgaccg 420
agaacgcagc atccacgaga atgccacggg tgacctggcc accagcagga atgcagcgga 480
ttcctctgtc ccaagtgtc ccagaaggca ggattctgaa gaccactcca gcgatatgtt 540

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311

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caactatgaa gaatactgca ccgccaacgc agtcactggg ccttgccgtg catccttccc 600
acgctggtac tttgacgtgg agaggaactc ctgcaataac ttcactatg gaggctgccg 660
gggcaataag aacagctacc gctctgagga ggcctgcatg ctccgctgct tccgccagca 720
ggagaatcct cccctgcccc ttggctcaaa ggtggtggtt ctggcggggc tgttcgtgat 780
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ccaggagcgt gccctgcgca ccgtctggag ctccggagat gacaaggagc agctggtgaa 900
gaacacatat gtcctgtgac cgccctgtcg ccaagaggac tggggaaggg aggggagact 960
atgtgtgagc tttttttaa tagagggatt gactcggatt tgagtgatca ttagggctga 1020
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tggaatcct ctaggaggct cctcctcgca tggcctgcag tctggcagca gccccgagtt 1140
gtttcctcgc tgatcgattt ctttcctcca ggtagagttt tctttgctta tgttgaattc 1200
cattgcctct tttctcatca cagaagtgat gttggaatcg tttcttttgt ttgtctgatt 1260
tatggttttt ttaagtataa acaaaagtgt tttattagca ttctgaaaga aggaaagtaa 1320
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aggtgtccca ttctagaaat agaccctca aaatagcgtc tttcagatct ttttgaatga 1500
atccacaaga tgaaataaat gtcctattac tgaaaaaaa aaaaaaaagg gcggccgc 1558

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&lt;210&gt; 304

&lt;211&gt; 195

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; VARIANT

&lt;222&gt; (1)...(195)

&lt;223&gt; Xaa = Any Amino Acid

&lt;400&gt; 304

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Met Ala Gln Leu Cys Gly Leu Arg Arg Ser Arg Ala Phe Leu Ala Leu
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Leu Gly Ser Leu Leu Ser Gly Val Leu Ala Ala Asp Arg Glu Arg
      20             25             30
Ser Ile His Glu Asn Ala Thr Gly Asp Leu Ala Thr Ser Arg Asn Ala
      35             40             45
Ala Asp Ser Ser Val Pro Ser Ala Pro Arg Arg Gln Asp Ser Glu Asp
      50             55             60
His Ser Ser Asp Met Phe Asn Tyr Glu Glu Tyr Cys Thr Ala Asn Ala
      65             70             75             80
Val Thr Gly Pro Cys Arg Ala Ser Phe Pro Arg Trp Tyr Phe Asp Val
      85             90             95
Glu Arg Asn Ser Cys Asn Asn Phe Ile Tyr Gly Gly Cys Arg Gly Asn
      100            105            110
Lys Asn Ser Tyr Arg Ser Glu Glu Ala Cys Met Leu Arg Cys Phe Arg
      115            120            125
Gln Gln Glu Asn Pro Pro Leu Pro Leu Gly Ser Lys Val Val Xaa Leu
      130            135            140
Ala Gly Leu Phe Val Met Val Leu Ile Leu Phe Leu Gly Ala Ser Met
      145            150            155            160
Val Tyr Leu Ile Arg Val Ala Arg Arg Asn Gln Glu Arg Ala Leu Arg
      165            170            175
Thr Val Trp Ser Ser Gly Asp Asp Lys Glu Gln Leu Val Lys Asn Thr
      180            185            190
Tyr Val Leu
      195

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&lt;210&gt; 305

&lt;211&gt; 3079

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 305

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acgcgggcgc agggctacac cgagttcagc ctccgcgtgg agggcgaccc cgacttctac 240
aagccgggaa ccagctaccg cgtaacactt tcagctgctc ctccctccta cttcagagga 300
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gatgagggct ctctgaccaa gaaactttgt gaacaagatt ccacatttga tggggtgact 600
gacaaaccca tcttagactg ctgtgcctgc ggaactgcca agtacagact cacattttat 660
gggaattggg ccgagaagac acacccaaag gattaccctc gtcgggcca cactgggtct 720
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313

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 <211> 807  
 <212> PRT  
 <213> Homo sapiens

<400> 306

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314

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&lt;210&gt; 307

&lt;211&gt; 5108

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 307

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316

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&lt;210&gt; 308

&lt;211&gt; 934

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 308

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20          25          30
Cys Ala Gly Gly Ser Gly Gln Asn Gln Pro Ser Leu Leu Pro Leu Leu
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Arg Arg Gly Pro Pro Leu Leu Ala Leu Leu Ser Phe Ala Trp Leu Ser
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Ser Ala Gln Leu Ser Ala Ala Pro Arg Pro Pro Ser Arg Gly Gly His
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Pro Pro Pro Gly Arg Ala Phe Val Gly Thr Thr Ser Gly Arg Ser Arg
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<211> 5471
<212> DNA
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320

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&lt;210&gt; 310

&lt;211&gt; 835

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 310

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          20          25          30
Cys Ala Gly Gly Ser Gly Gln Asn Gln Pro Ser Leu Leu Pro Leu Leu
          35          40          45
Arg Arg Gly Pro Pro Leu Leu Ala Leu Leu Ser Phe Ala Trp Leu Ser
          50          55          60
Ser Ala Gln Leu Ser Ala Ala Pro Arg Pro Pro Ser Arg Gly Gly His
          65          70          75          80
Gly Leu Arg Val Ala Asp Ala Ser Ser Glu Leu Pro Leu Ser Ala Ala
          85          90          95
Pro Pro Pro Gly Arg Ala Phe Val Gly Thr Thr Ser Gly Arg Ser Arg
          100          105          110
Val Ala Lys Ala Cys Gly Arg Gly Thr Lys Leu Gly Ala Ala Lys Met
          115          120          125
Arg Leu Ser Pro Ala Pro Leu Lys Leu Ser Arg Thr Pro Ala Leu Leu
          130          135          140
Ala Leu Ala Leu Pro Leu Ala Ala Ala Leu Ala Phe Ser Asp Glu Thr
          145          150          155          160
Leu Asp Lys Val Pro Lys Ser Glu Gly Tyr Cys Ser Arg Ile Leu Arg
          165          170          175
Ala Gln Gly Thr Arg Arg Glu Gly Tyr Thr Glu Phe Ser Leu Arg Val
          180          185          190
Glu Gly Asp Pro Asp Phe Tyr Lys Pro Gly Thr Ser Tyr Arg Val Thr
          195          200          205
Leu Ser Ala Ala Pro Pro Ser Tyr Phe Arg Gly Phe Thr Leu Ile Ala
          210          215          220
Leu Arg Glu Asn Arg Glu Gly Asp Lys Glu Glu Asp His Ala Gly Thr
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321

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 275 280 285  
 Ser Ile Val Gln Lys Arg Ile Ile Tyr Phe Gln Asp Glu Gly Ser Leu  
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 Thr Lys Lys Leu Cys Glu Gln Asp Ser Thr Phe Asp Gly Val Thr Asp  
 305 310 315 320  
 Lys Pro Ile Leu Asp Cys Cys Ala Cys Gly Thr Ala Lys Tyr Arg Leu  
 325 330 335  
 Thr Phe Tyr Gly Asn Trp Ser Glu Lys Thr His Pro Lys Asp Tyr Pro  
 340 345 350  
 Arg Arg Ala Asn His Trp Ser Ala Ile Ile Gly Gly Ser His Ser Lys  
 355 360 365  
 Asn Tyr Val Leu Trp Glu Tyr Gly Gly Tyr Ala Ser Glu Gly Val Lys  
 370 375 380  
 Gln Val Ala Glu Leu Gly Ser Pro Val Lys Met Glu Glu Ile Arg  
 385 390 395 400  
 Gln Gln Ser Asp Glu Val Leu Thr Val Ile Lys Ala Lys Ala Gln Trp  
 405 410 415  
 Pro Ala Trp Gln Pro Leu Asn Val Arg Ala Ala Pro Ser Ala Glu Phe  
 420 425 430  
 Ser Val Asp Arg Thr Arg His Leu Met Ser Phe Leu Thr Met Met Gly  
 435 440 445  
 Pro Ser Pro Asp Trp Asn Val Gly Leu Ser Ala Glu Asp Leu Cys Thr  
 450 455 460  
 Lys Glu Cys Gly Trp Val Gln Lys Val Val Gln Asp Leu Ile Pro Trp  
 465 470 475 480  
 Asp Ala Gly Thr Asp Ser Gly Val Thr Tyr Glu Ser Pro Asn Lys Pro  
 485 490 495  
 Thr Ile Pro Gln Glu Lys Ile Arg Pro Leu Thr Ser Leu Asp His Pro  
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 Gln Ser Pro Phe Tyr Asp Pro Glu Gly Gly Ser Ile Thr Gln Val Ala  
 515 520 525  
 Arg Val Val Ile Glu Arg Ile Ala Arg Lys Gly Glu Gln Cys Asn Ile  
 530 535 540  
 Val Pro Asp Asn Val Asp Asp Ile Val Ala Asp Leu Ala Pro Glu Glu  
 545 550 555 560  
 Lys Asp Glu Asp Asp Thr Pro Glu Thr Cys Ile Tyr Ser Asn Trp Ser  
 565 570 575  
 Pro Trp Ser Ala Cys Ser Ser Ser Thr Cys Asp Lys Gly Lys Arg Met  
 580 585 590  
 Arg Gln Arg Met Leu Lys Ala Gln Leu Asp Leu Ser Val Pro Cys Pro  
 595 600 605  
 Asp Thr Gln Asp Phe Gln Pro Cys Met Gly Pro Gly Cys Ser Asp Glu  
 610 615 620  
 Asp Gly Ser Thr Cys Thr Met Ser Glu Trp Ile Thr Trp Ser Pro Cys  
 625 630 635 640  
 Ser Ile Ser Cys Gly Met Gly Met Arg Ser Arg Glu Arg Tyr Val Lys  
 645 650 655  
 Gln Phe Pro Glu Asp Gly Ser Val Cys Thr Leu Pro Thr Glu Glu Thr  
 660 665 670  
 Glu Lys Cys Thr Val Asn Glu Glu Cys Ser Pro Ser Ser Cys Leu Met  
 675 680 685  
 Thr Glu Trp Gly Glu Trp Asp Glu Cys Ser Ala Thr Cys Gly Met Gly  
 690 695 700

322

Met Lys Lys Arg His Arg Met Ile Lys Met Asn Pro Ala Asp Gly Ser  
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 Met Cys Lys Ala Glu Thr Ser Gln Ala Glu Lys Cys Met Met Pro Glu  
 725 730 735  
 Cys His Thr Ile Pro Cys Leu Leu Ser Pro Trp Ser Glu Trp Ser Asp  
 740 745 750  
 Cys Ser Val Thr Cys Gly Lys Gly Met Arg Thr Arg Gln Arg Met Leu  
 755 760 765  
 Lys Ser Leu Ala Glu Leu Gly Asp Cys Asn Glu Asp Leu Glu Gln Val  
 770 775 780  
 Glu Lys Cys Met Leu Pro Glu Cys Pro Ile Asp Cys Glu Leu Thr Glu  
 785 790 795 800  
 Trp Ser Gln Trp Ser Glu Cys Asn Lys Ser Cys Gly Lys Gly His Val  
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 820 825 830  
 Leu Glu Ser  
 835

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 <211> 3112  
 <212> DNA  
 <213> Homo sapiens

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323

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&lt;210&gt; 312

&lt;211&gt; 782

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 312

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Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
  35          40          45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
  50          55          60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
  65          70          75          80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
  85          90          95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
  100         105         110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
  115         120         125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
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Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
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Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
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Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
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Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
  195         200         205
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His	Thr	Tyr	Arg	Cys	Leu	Asn	Gly	Leu	Cys	Leu	Ser	Lys	Gly	Asn	Pro	
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Gly	Thr	Asp	Ala	Asp	Glu	Gly	Glu	Trp	Pro	Trp	Gln	Val	Ser	Leu	His	
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Ala	Leu	Gly	Gln	Gly	His	Ile	Cys	Gly	Ala	Ser	Leu	Ile	Ser	Pro	Asn	
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Trp	Leu	Val	Ser	Ala	Ala	His	Cys	Tyr	Ile	Asp	Asp	Arg	Gly	Phe	Arg	
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325

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	725		730		735	
Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly Val Val Ser						
	740		745		750	
Trp Gly Asp Gly Cys Ala Gln Arg Asn Lys Pro Gly Val Tyr Thr Arg						
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 <212> DNA  
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326

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&lt;210&gt; 314

&lt;211&gt; 323

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 314

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Leu	Leu	Leu	Val	Leu	Ala	Ala	Val	Thr	Gly	His	Thr	Ala	Ala	Gln	Asp
			20					25				30			
Asn	Cys	Thr	Cys	Pro	Thr	Asn	Lys	Met	Thr	Val	Cys	Ser	Pro	Asp	Gly
			35				40					45			
Pro	Gly	Gly	Arg	Cys	Gln	Cys	Arg	Ala	Leu	Gly	Ser	Gly	Met	Ala	Val
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Asp	Cys	Ser	Thr	Leu	Thr	Ser	Lys	Cys	Leu	Leu	Leu	Lys	Ala	Arg	Met
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Ser	Ala	Pro	Lys	Asn	Ala	Arg	Thr	Leu	Val	Arg	Pro	Ser	Glu	His	Ala
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Cys	Asp	Glu	Leu	Val	Arg	Thr	His	His	Ile	Leu	Ile	Asp	Leu	Arg	His
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Arg	Pro	Thr	Ala	Gly	Ala	Phe	Asn	His	Ser	Asp	Leu	Asp	Ala	Glu	Leu
			165					170						175	
Arg	Arg	Leu	Phe	Arg	Glu	Arg	Tyr	Arg	Leu	His	Pro	Lys	Phe	Val	Ala
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Val	Ala	Gly	Met	Ala	Val	Leu	Val	Ile	Thr	Asn	Arg	Arg	Lys	Ser	Gly
			290			295					300				
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Pro	Ser	Leu													

&lt;210&gt; 315

327

&lt;211&gt; 1142

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 315

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1142

&lt;210&gt; 316

&lt;211&gt; 235

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 316

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20          25          30
Ala Glu Ile Cys Leu Leu Pro Leu Asp Tyr Gly Pro Cys Arg Ala Leu
35          40          45
Leu Leu Arg Tyr Tyr Tyr Asp Arg Tyr Thr Gln Ser Cys Arg Gln Phe
50          55          60
Leu Tyr Gly Gly Cys Glu Gly Asn Ala Asn Asn Phe Tyr Thr Trp Glu
65          70          75          80
Ala Cys Asp Asp Ala Cys Trp Arg Ile Glu Lys Val Pro Lys Val Cys
85          90          95
Arg Leu Gln Val Ser Val Asp Asp Gln Cys Glu Gly Ser Thr Glu Lys
100         105         110
Tyr Phe Phe Asn Leu Ser Ser Met Thr Cys Glu Lys Phe Phe Ser Gly
115         120         125
Gly Cys His Arg Asn Arg Ile Glu Asn Arg Phe Pro Asp Glu Ala Thr
130         135         140
Cys Met Gly Phe Cys Ala Pro Lys Lys Ile Pro Ser Phe Cys Tyr Ser
145         150         155         160
Pro Lys Asp Glu Gly Leu Cys Ser Ala Asn Val Thr Arg Tyr Tyr Phe
165         170         175
Asn Pro Arg Tyr Arg Thr Cys Asp Ala Phe Thr Tyr Thr Gly Cys Gly
180         185         190
Gly Asn Asp Asn Asn Phe Val Ser Arg Glu Asp Cys Lys Arg Ala Cys
195         200         205

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328

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<210> 318

329

&lt;211&gt; 428

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 318

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          20           25           30
Gly Ile Pro Ile Ile Ile Ala Leu Leu Ser Leu Ala Ser Ile Ile Ile
      35           40           45
Val Val Val Leu Ile Lys Val Ile Leu Asp Lys Tyr Tyr Phe Leu Cys
      50           55           60
Gly Gln Pro Leu His Phe Ile Pro Arg Lys Gln Leu Cys Asp Gly Glu
      65           70           75           80
Leu Asp Cys Pro Leu Gly Glu Asp Glu Glu His Cys Val Lys Ser Phe
          85           90           95
Pro Glu Gly Pro Ala Val Ala Val Arg Leu Ser Lys Asp Arg Ser Thr
          100          105          110
Leu Gln Val Leu Asp Ser Ala Thr Gly Asn Trp Phe Ser Ala Cys Phe
          115          120          125
Asp Asn Phe Thr Glu Ala Leu Ala Glu Thr Ala Cys Arg Gln Met Gly
          130          135          140
Tyr Ser Ser Lys Pro Thr Phe Arg Ala Val Glu Ile Gly Pro Asp Gln
          145          150          155          160
Asp Leu Asp Val Val Glu Ile Thr Glu Asn Ser Gln Glu Leu Arg Met
          165          170          175
Arg Asn Ser Ser Gly Pro Cys Leu Ser Gly Ser Leu Val Ser Leu His
          180          185          190
Cys Leu Ala Cys Gly Lys Ser Leu Lys Thr Pro Arg Val Val Gly Gly
          195          200          205
Glu Glu Ala Ser Val Asp Ser Trp Pro Trp Gln Val Ser Ile Gln Tyr
          210          215          220
Asp Lys Gln His Val Cys Gly Gly Ser Ile Leu Asp Pro His Trp Val
          225          230          235          240
Leu Thr Ala Ala His Cys Phe Arg Lys His Thr Asp Val Phe Asn Trp
          245          250          255
Lys Val Arg Ala Gly Ser Asp Lys Leu Gly Ser Phe Pro Ser Leu Ala
          260          265          270
Val Ala Lys Ile Ile Ile Ile Glu Phe Asn Pro Met Tyr Pro Lys Asp
          275          280          285
Asn Asp Ile Ala Leu Met Lys Leu Gln Phe Pro Leu Thr Phe Ser Gly
          290          295          300
Thr Val Arg Pro Ile Cys Leu Pro Phe Phe Asp Glu Glu Leu Thr Pro
          305          310          315          320
Ala Thr Pro Leu Trp Ile Ile Gly Trp Gly Phe Thr Lys Gln Asn Gly
          325          330          335
Gly Lys Met Ser Asp Ile Leu Leu Gln Ala Ser Val Gln Val Ile Asp
          340          345          350
Ser Thr Arg Cys Asn Ala Asp Asp Ala Tyr Gln Gly Glu Val Thr Glu
          355          360          365
Lys Met Met Cys Ala Gly Ile Pro Glu Gly Gly Val Asp Thr Cys Gln
          370          375          380
Gly Asp Ser Gly Gly Pro Leu Met Tyr Gln Ser Asp Gln Trp His Val
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420

425

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<212> DNA  
<213> Homo sapiens

&lt;400&gt; 319

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331

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tgggataata aatgaacaca aaatttaaaa aaaaaaaaaa aaataaaaaa 3529

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&lt;210&gt; 320

&lt;211&gt; 444

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 320

```

Met Ile Glu Asp Asn Lys Glu Asn Lys Asp His Ser Leu Glu Arg Gly
 1           5           10           15
Arg Ala Ser Leu Ile Phe Ser Leu Lys Asn Glu Val Gly Gly Leu Ile
      20           25           30
Lys Ala Leu Lys Ile Phe Gln Glu Lys His Val Asn Leu Leu His Ile
      35           40           45
Glu Ser Arg Lys Ser Lys Arg Arg Asn Ser Glu Phe Glu Ile Phe Val
      50           55           60
Asp Cys Asp Ile Asn Arg Glu Gln Leu Asn Asp Ile Phe His Leu Leu
      65           70           75           80
Lys Ser His Thr Asn Val Leu Ser Val Asn Leu Pro Asp Asn Phe Thr
      85           90           95
Leu Lys Glu Asp Gly Met Glu Thr Val Pro Trp Phe Pro Lys Lys Ile
      100          105          110
Ser Asp Leu Asp His Cys Ala Asn Arg Val Leu Met Tyr Gly Ser Glu
      115          120          125
Leu Asp Ala Asp His Pro Gly Phe Lys Asp Asn Val Tyr Arg Lys Arg
      130          135          140
Arg Lys Tyr Phe Ala Asp Leu Ala Met Asn Tyr Lys His Gly Asp Pro
      145          150          155          160
Ile Pro Lys Val Glu Phe Thr Glu Glu Glu Ile Lys Thr Trp Gly Thr
      165          170          175
Val Phe Gln Glu Leu Asn Lys Leu Tyr Pro Thr His Ala Cys Arg Glu
      180          185          190
Tyr Leu Lys Asn Leu Pro Leu Leu Ser Lys Tyr Cys Gly Tyr Arg Glu
      195          200          205
Asp Asn Ile Pro Gln Leu Glu Asp Val Ser Asn Phe Leu Lys Glu Arg
      210          215          220
Thr Gly Phe Ser Ile Arg Pro Val Ala Gly Tyr Leu Ser Pro Arg Asp
      225          230          235          240
Phe Leu Ser Gly Leu Ala Phe Arg Val Phe His Cys Thr Gln Tyr Val
      245          250          255
Arg His Ser Ser Asp Pro Phe Tyr Thr Pro Glu Pro Asp Thr Cys His
      260          265          270
Glu Leu Leu Gly His Val Pro Leu Leu Ala Glu Pro Ser Phe Ala Gln
      275          280          285
Phe Ser Gln Glu Ile Gly Leu Ala Ser Leu Gly Ala Ser Glu Glu Ala
      290          295          300
Val Gln Lys Leu Ala Thr Cys Tyr Phe Phe Thr Val Glu Phe Gly Leu
      305          310          315          320
Cys Lys Gln Asp Gly Gln Leu Arg Val Phe Gly Ala Gly Leu Leu Ser

```

1

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333

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&lt;210&gt; 322

&lt;211&gt; 466

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 322

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Met Ile Glu Asp Asn Lys Glu Asn Lys Asp His Ser Leu Glu Arg Gly
1      5      10      15
Arg Ala Ser Leu Ile Phe Ser Leu Lys Asn Glu Val Gly Gly Leu Ile
20     25     30
Lys Ala Leu Lys Ile Phe Gln Glu Lys His Val Asn Leu Leu His Ile
35     40     45
Glu Ser Arg Lys Ser Lys Arg Arg Asn Ser Glu Phe Glu Ile Phe Val
50     55     60
Asp Cys Asp Ile Asn Arg Glu Gln Leu Asn Asp Ile Phe His Leu Leu
65     70     75     80
Lys Ser His Thr Asn Val Leu Ser Val Asn Leu Pro Asp Asn Phe Thr
85     90     95
Leu Lys Glu Asp Gly Met Glu Thr Val Pro Trp Phe Pro Lys Lys Ile
100    105    110
Ser Asp Leu Asp His Cys Ala Asn Arg Val Leu Met Tyr Gly Ser Glu
115    120    125
Leu Asp Ala Asp His Pro Gly Phe Lys Asp Asn Val Tyr Arg Lys Arg
130    135    140
Arg Lys Tyr Phe Ala Asp Leu Ala Met Asn Tyr Lys His Gly Asp Pro
145    150    155    160
Ile Pro Lys Val Glu Phe Thr Glu Glu Glu Ile Lys Thr Trp Gly Thr
165    170    175
Val Phe Gln Glu Leu Asn Lys Leu Tyr Pro Thr His Ala Cys Arg Glu
180    185    190
Tyr Leu Lys Asn Leu Pro Leu Leu Ser Lys Tyr Cys Gly Tyr Arg Glu
195    200    205
Asp Asn Ile Pro Gln Leu Glu Asp Val Ser Asn Phe Leu Lys Glu Arg

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334

210	215	220
Thr Gly Phe Ser Ile Arg Pro Val Ala Gly Tyr Leu Ser Pro Arg Asp		
225	230	235
Phe Leu Ser Gly Leu Ala Phe Arg Val Phe His Cys Thr Gln Tyr Val		
	245	250
Arg His Ser Ser Asp Pro Phe Tyr Thr Pro Glu Pro Asp Thr Cys His		
	260	265
Glu Leu Leu Gly His Val, Pro Leu Leu Ala Glu Pro Ser Phe Ala Gln		
	275	280
Phe Ser Gln Glu Ile Gly Leu Ala Ser Leu Gly Ala Ser Glu Glu Ala		
	290	295
Val Gln Lys Leu Ala Thr Cys Tyr Phe Phe Thr Val Glu Phe Gly Leu		
305	310	315
Cys Lys Gln Asp Gly Gln Leu Arg Val Phe Gly Ala Gly Leu Leu Ser		
	325	330
Ser Ile Ser Glu Leu Lys His Ala Leu Ser Gly His Ala Lys Val Lys		
	340	345
Pro Phe Asp Pro Lys Ile Thr Cys Lys Gln Glu Cys Leu Ile Thr Thr		
	355	360
Phe Gln Asp Val Tyr Phe Val Ser Glu Ser Phe Glu Asp Ala Lys Glu		
	370	375
Lys Met Arg Glu Phe Thr Lys Thr Ile Lys Arg Pro Phe Gly Val Lys		
385	390	395
Tyr Asn Pro Tyr Thr Arg Ser Ile Gln Ile Leu Lys Asp Thr Lys Ser		
	405	410
Ile Thr Ser Ala Met Asn Glu Leu Gln His Asp Leu Asp Val Val Ser		
	420	425
Asp Ala Leu Ala Lys Ser Leu Asn Glu Asp Val Leu Gln Val Ser Val		
	435	440
Phe Ala Leu Leu Leu Phe Leu Pro Ser Leu His Gly Glu Cys His Pro.		
	450	455
Asp Thr		460
465		

&lt;210&gt; 323

&lt;211&gt; 1154

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 323

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335

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 aaaaaaaaaa aagt 1154

<210> 324  
 <211> 258  
 <212> PRT  
 <213> Homo sapiens

<400> 324  
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 20 25 30  
 Ser Ile Asp Gly Ala Ser Phe Leu Lys Ile Phe Gly Pro Leu Ser Ser  
 35 40 45  
 Ser Ala Met Gln Phe Val Asn Val Gly Tyr Phe Leu Ile Ala Ala Gly  
 50 55 60  
 Val Val Val Phe Ala Leu Gly Phe Leu Gly Cys Tyr Gly Ala Lys Thr  
 65 70 75 80  
 Glu Ser Lys Cys Ala Leu Val Thr Phe Phe Phe Ile Leu Leu Leu Ile  
 85 90 95  
 Phe Ile Ala Glu Val Ala Ala Ala Val Val Ala Leu Val Tyr Thr Thr  
 100 105 110  
 Met Ala Glu His Phe Leu Thr Leu Leu Val Val Pro Ala Ile Lys Lys  
 115 120 125  
 Asp Tyr Gly Ser Gln Glu Asp Phe Thr Gln Val Trp Asn Thr Thr Met  
 130 135 140  
 Lys Gly Leu Lys Cys Cys Gly Phe Thr Asn Tyr Thr Asp Phe Glu Asp  
 145 150 155 160  
 Ser Pro Tyr Phe Lys Glu Asn Ser Ala Phe Pro Pro Phe Cys Cys Asn  
 165 170 175  
 Asp Asn Val Thr Asn Thr Ala Asn Glu Thr Cys Thr Lys Gln Lys Ala  
 180 185 190  
 His Asp Gln Lys Val Glu Gly Cys Phe Asn Gln Leu Leu Tyr Asp Ile  
 195 200 205  
 Arg Thr Asn Ala Val Thr Val Gly Gly Val Ala Ala Gly Ile Gly Gly  
 210 215 220  
 Leu Glu Phe Phe Ser Asn Ser Ala Arg Arg Pro Pro Leu Pro Glu Ser  
 225 230 235 240  
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 245 250 255  
 Pro Pro

<210> 325  
 <211> 1076  
 <212> DNA  
 <213> Homo sapiens

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336

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&lt;210&gt; 326

&lt;211&gt; 241

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 326

Met	Gln	Cys	Phe	Ser	Phe	Ile	Lys	Thr	Met	Met	Ile	Leu	Phe	Asn	Leu
1			5						10					15	
Leu	Ile	Phe	Leu	Cys	Gly	Ala	Ala	Leu	Leu	Ala	Val	Gly	Ile	Trp	Val
			20					25					30		
Ser	Ile	Asp	Gly	Ala	Ser	Phe	Leu	Lys	Ile	Phe	Gly	Pro	Leu	Ser	Ser
		35					40					45			
Ser	Ala	Met	Gln	Phe	Val	Asn	Val	Gly	Tyr	Phe	Leu	Ile	Ala	Ala	Gly
	50					55					60				
Val	Val	Val	Phe	Ala	Leu	Gly	Phe	Leu	Gly	Cys	Tyr	Gly	Ala	Lys	Thr
	65				70				75					80	
Glu	Ser	Lys	Cys	Ala	Leu	Val	Thr	Phe	Phe	Phe	Ile	Leu	Leu	Leu	Ile
			85					90					95		
Phe	Ile	Ala	Glu	Val	Ala	Ala	Ala	Val	Val	Ala	Leu	Val	Tyr	Thr	Thr
		100						105					110		
Met	Ala	Glu	His	Phe	Leu	Thr	Leu	Leu	Val	Val	Pro	Ala	Ile	Lys	Lys
		115					120					125			
Asp	Tyr	Gly	Ser	Gln	Glu	Asp	Phe	Thr	Gln	Val	Trp	Asn	Thr	Thr	Met
	130					135					140				
Lys	Gly	Leu	Lys	Cys	Cys	Gly	Phe	Thr	Asn	Tyr	Thr	Asp	Phe	Glu	Asp
	145				150				155					160	
Ser	Pro	Tyr	Phe	Lys	Glu	Asn	Ser	Ala	Phe	Pro	Pro	Phe	Cys	Cys	Asn
			165					170					175		
Asp	Asn	Val	Thr	Asn	Thr	Ala	Asn	Glu	Thr	Cys	Thr	Glu	Gln	Lys	Ala
		180						185					190		
His	Asp	Gln	Lys	Val	Glu	Gly	Cys	Phe	Asn	Gln	Leu	Leu	Tyr	Asp	Ile
	195						200						205		
Arg	Thr	Asn	Ala	Val	Thr	Val	Gly	Gly	Val	Ala	Ala	Gly	Ile	Gly	Gly
	210					215				220					
Leu	Glu	Leu	Ala	Ala	Met	Ile	Val	Ser	Met	Tyr	Leu	Tyr	Cys	Asn	Leu
	225				230					235					240
Gln															

&lt;210&gt; 327

&lt;211&gt; 2244

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

337

&lt;400&gt; 327

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&lt;210&gt; 328

&lt;211&gt; 498

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 328

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Cys Gly Ser Arg Leu Gln Pro Pro Gly Pro Glu Thr Ser Ser Phe Ser
20          25          30
Ser Gln Thr Lys Gln Ser Ser Ile Ile Ile Gln Pro Arg Gln Cys Thr
35          40          45
Glu Gln Arg Phe Ser Ala Ser Ser Thr Leu Ser Ser His Ile Thr Met
50          55          60
Ser Ser Ser Ala Phe Pro Ala Ser Pro Gln Gln His Ala Gly Ser Asn
65          70          75          80
Pro Gly Gln Arg Val Thr Thr Thr Tyr Asn Gln Ser Pro Ala Ser Phe
85          90          95

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338

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 Ile Asn Ala Lys Pro Ser Gln Thr Ala Asn Ala Lys Pro Ile Pro Arg  
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 Thr Pro Asp His Glu Ile Gln Gly Ser Lys Glu Ala Leu Ile Gln Asp  
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 Leu Glu Arg Lys Leu Lys Cys Lys Asp Thr Leu Leu His Asn Gly Asn  
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 Asp Ala Ile Gln Glu Lys Phe Tyr Pro Pro Arg Phe Ile Gln Val Pro  
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 Asp Asn Thr Gly Arg Val Thr Leu Leu Ile Lys Asp Val Asn Lys Lys  
                   405                  410                  415  
 Asp Ala Gly Trp Tyr Thr Val Ser Ala Val Asn Glu Ala Gly Val Thr  
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                   450                  455                  460  
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 Glu Leu

&lt;210&gt; 329

&lt;211&gt; 3649

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 329

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340

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&lt;210&gt; 330

&lt;211&gt; 812

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 330

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Leu	Asn	Thr	Ile	Ala	Glu	Gly	Asp	Asn	Val	Tyr	Ala	Phe	Gln	Val	Pro
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Pro	Ser	Pro	Ser	Gln	Gly	Thr	Leu	Ser	Ala	His	Pro	Leu	Gly	Leu	Ser
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Ala	Ser	Pro	Arg	Leu	Ala	Ala	Arg	Glu	Gly	Gln	Arg	Phe	Ser	Leu	Ser
65				70						75				80	
Leu	His	Ser	Glu	Ser	Lys	Val	Leu	Ile	Leu	Phe	Cys	Asn	Leu	Val	Gly
			85						90				95		
Ser	Gly	Gln	Gln	Ala	Ser	Arg	Phe	Gly	Pro	Pro	Phe	Leu	Ile	Arg	Glu
			100					105					110		
Asp	Arg	Ala	Val	Ser	Trp	Ala	Gln	Leu	Gln	Gln	Ser	Ile	Leu	Ser	Lys
			115				120					125			
Val	Arg	His	Leu	Met	Lys	Ser	Glu	Ala	Pro	Val	Gln	Asn	Leu	Gly	Ser
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Leu	Phe	Ser	Ile	Arg	Val	Val	Gly	Leu	Ser	Val	Ala	Cys	Ser	Tyr	Leu
145				150						155				160	
Ser	Pro	Lys	Asp	Ser	Arg	Pro	Leu	Cys	His	Trp	Ala	Val	Asp	Arg	Val
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Leu	His	Leu	Arg	Arg	Pro	Gly	Gly	Pro	Pro	His	Val	Lys	Leu	Ala	Val
			180					185					190		
Glu	Trp	Asp	Ser	Ser	Val	Lys	Glu	Arg	Leu	Phe	Gly	Ser	Leu	Gln	Glu
			195				200					205			
Glu	Arg	Ala	Gln	Asp	Ala	Asp	Ser	Val	Trp	Gln	Gln	Gln	Gln	Ala	His
			210			215					220				
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225				230						235				240	
Glu	Glu	Gln	Leu	Ala	Gln	Asp	Asp	Ala	Trp	Lys	Cys	Pro	His	Cys	Gln
			245						250					255	
Val	Leu	Gln	Gln	Gly	Met	Val	Lys	Leu	Ser	Leu	Trp	Thr	Leu	Pro	Asp
			260					265					270		
Ile	Leu	Ile	His	Leu	Lys	Arg	Phe	Cys	Gln	Val	Gly	Glu	Arg	Arg	
			275				280					285			
Asn	Lys	Leu	Ser	Thr	Leu	Val	Lys	Phe	Pro	Leu	Ser	Gly	Leu	Asn	Met
			290			295					300				
Ala	Pro	His	Val	Ala	Gln	Arg	Ser	Thr	Ser	Pro	Glu	Ala	Gly	Leu	Gly
305				310						315				320	
Pro	Trp	Pro	Ser	Trp	Lys	Gln	Pro	Asp	Cys	Leu	Pro	Thr	Ser	Tyr	Pro
			325						330					335	
Leu	Asp	Phe	Leu	Tyr	Asp	Leu	Tyr	Ala	Val	Cys	Asn	His	His	Gly	Asn
			340				345					350			
Leu	Gln	Gly	Gly	His	Tyr	Thr	Ala	Tyr	Cys	Arg	Asn	Ser	Leu	Asp	Gly
			355				360					365			

341

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 Glu Val Asn Thr Arg Gly Ala Tyr Ile Leu Phe Tyr Gln Lys Arg Asn  
 385 390 395 400  
 Ser Ile Pro Pro Trp Ser Ala Ser Ser Ser Met Arg Gly Ser Thr Ser  
 405 410 415  
 Ser Ser Leu Ser Asp His Trp Leu Leu Arg Leu Gly Ser His Ala Gly  
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 Ser Thr Arg Gly Ser Leu Leu Ser Trp Ser Ser Ala Pro Cys Pro Ser  
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 Gly Arg Ser Ile Ser Met Lys Ala Pro Thr Thr Ser Arg Ala Lys Gln  
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 Gly Pro Phe Lys Thr Met Pro Leu Arg Trp Ser Phe Gly Ser Lys Glu  
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 Lys Pro Pro Gly Ala Ser Val Glu Leu Val Glu Tyr Leu Glu Ser Arg  
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 595 600 605  
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 610 615 620  
 Met Pro Ser Val Glu His Glu Lys Pro Ala Arg Pro Glu Gly Gln Lys  
 625 630 635 640  
 Ala Met Asn Trp Lys Glu Ser Phe Gln Met Gly Ser Lys Ser Ser Pro  
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 Pro Ser Pro Tyr Met Gly Phe Ser Gly Asn Ser Lys Asp Ser Arg Arg  
 660 665 670  
 Gly Thr Ser Glu Leu Asp Arg Pro Leu Gln Gly Thr Leu Thr Leu Leu  
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 Arg Ser Val Phe Arg Lys Lys Glu Asn Arg Arg Asn Glu Arg Ala Glu  
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 Val Ser Pro Gln Val Pro Pro Val Ser Leu Val Ser Gly Gly Leu Ser  
 705 710 715 720  
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 Pro Glu Gly Leu Ala Arg Gly Leu Gly Ser Arg Leu Glu Arg Asp Val  
 740 745 750  
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 755 760 765  
 Pro Arg Gly Ser Ala Leu Gly Met Ser Gln Arg Thr Val Pro Gly Glu  
 770 775 780  
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342

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 <213> Homo sapiens

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 <212> PRT  
 <213> Homo sapiens

<400> 332  
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 Gly Glu Asp Gly Ile Gln Ser Cys Thr Phe Glu Pro Asp Ile Lys Leu  
 50 55 60  
 Ser Asp Ile Val Ile Gln Trp Leu Lys Glu Gly Val Leu Gly Leu Val  
 65 70 75 80  
 His Glu Phe Lys Glu Gly Lys Asp Glu Leu Ser Glu Gln Asp Glu Met  
 85 90 95  
 Phe Arg Gly Arg Thr Ala Val Phe Ala Asp Gln Val Ile Val Gly Asn  
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343

Ala Ser Leu Arg Leu Lys Asn Val Gln Leu Thr Asp Ala Gly Thr Tyr  
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 Lys Val Val Ser Val Leu Tyr Asn Val Thr Ile Asn Asn Thr Tyr Ser  
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&lt;210&gt; 333

&lt;211&gt; 1984

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 333

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344

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 aaaa 1984

&lt;210&gt; 334

&lt;211&gt; 258

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 334

Met	Phe	Tyr	Val	Ala	Glu	Pro	Lys	Gln	Val	Pro	His	Ile	Leu	Cys	Ser
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Pro	Ser	Met	Lys	Asn	Ile	Asn	Pro	Leu	Thr	Ala	Met	Ser	Tyr	Leu	Arg
			20					25					30		
Lys	Leu	Asp	Thr	Ser	Gly	Phe	Ser	Ser	Ile	Leu	Val	Thr	Leu	Thr	Lys
		35					40					45			
Ala	Ala	Val	Ala	Leu	Lys	Met	Gly	Asp	Leu	Asp	Met	His	Arg	Asn	Glu
	50					55					60				
Met	Lys	Ser	His	Ser	Glu	Met	Lys	Leu	Val	Cys	Gly	Phe	Ile	Leu	Glu
65					70					75				80	
Pro	Arg	Leu	Leu	Ile	Gln	Gln	Arg	Lys	Gly	Gln	Ile	Val	Pro	Thr	Glu
				85					90					95	
Leu	Ala	Leu	His	Leu	Lys	Glu	Thr	Gln	Pro	Gly	Leu	Leu	Val	Ala	Ser
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Val	Leu	Gly	Leu	Gln	Lys	Asn	Asn	Lys	Ile	Gly	Ile	Glu	Glu	Ala	Asp
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			165						170					175	
Arg	Leu	Ser	Lys	Arg	Gln	Pro	Pro	Asp	Thr	Thr	Pro	Leu	Arg	Thr	Ser
			180					185					190		
Glu	Asp	Leu	Ile	Asn	Ala	Cys	Ser	His	Tyr	Gly	Leu	Ile	Tyr	Pro	Trp
	195					200						205			
Val	His	Val	Val	Ile	Ser	Ser	Asp	Ser	Leu	Ala	Asp	Lys	Asn	Tyr	Thr
	210					215					220				
Glu	Asp	Leu	Ser	Lys	Leu	Gln	Leu	Pro	Leu	Phe	Arg	Ser	Trp	Ser	His
225					230					235				240	
Phe	Gln	Lys	Thr	Leu	Leu	Pro	Ala	Ser	Val	Ser	Met	Phe	Cys	Val	Val
				245					250					255	
His	Ala														

&lt;210&gt; 335

&lt;211&gt; 2180

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

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&lt;223&gt; n = A,T,C or G

345

&lt;400&gt; 335

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2180

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&lt;210&gt; 336

&lt;211&gt; 234

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 336

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20          25          30
Arg Arg Lys Leu Leu Met Asn Ser Glu Gln Arg Ile Asn Arg Ile Met
35          40          45
Gly Phe His Arg Pro Gly Ser Gly Ala Glu Glu Glu Ser Gln Thr Lys
50          55          60
Ser Lys Gln Gln Asp Ser Asp Lys Leu Asn Ser Leu Ser Val Pro Ser
65          70          75          80
Val Ser Lys Arg Val Val Leu Gly Asp Ser Val Ser Thr Gly Thr Thr
85          90          95

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346

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 Leu Glu Leu Arg Gln Arg Asn Arg Gly Asp Leu Thr Ala Asp Ser Val  
                   130                  135                  140  
 Gln Arg Gly Ser Arg His Gly Leu Glu Gln Tyr Leu Ser Arg Phe Glu  
                   145                  150                  155                  160  
 Glu Ala Met Lys Leu Arg Lys Gln Leu Ile Ser Glu Lys Pro Ser Gln  
                   165                  170                  175  
 Glu Asp Gly Asn Thr Thr Glu Glu Phe Asp Ser Phe Arg Ile Phe Arg  
                   180                  185                  190  
 Leu Val Gly Cys Ala Leu Leu Ala Leu Gly Val Arg Ala Phe Val Cys  
                   195                  200                  205  
 Lys Tyr Leu Ser Ile Phe Ala Pro Phe Leu Thr Leu Gln Leu Ala Leu  
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 His Gly Ile Ile Gln Ile Phe Ser Gln Glu  
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<210> 337  
 <211> 3695  
 <212> DNA  
 <213> Homo sapiens

<400> 337  
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 ccgtcgcgct cgaccccagc ggcatgcggc agccgcaggg gcccccgctc ccggggtcgg 180  
 cggcgcgggt gaacgtgagc ggatgttcac ttcttctcca caatgaatga gtgtcactat 240  
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 ggaacaaagc ttgtgattgt tttgtgtgtt gggacgtttt tctgcctgtt tatttttttt 360  
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 tacctgttgg ctaatttagc tgcgtccgat ttcttcgctg gaattgccta tgtattcctg 480  
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 taagagctcc agattaaacc tgatttttaa ctgaaggaac attctgagga aaaatactta 1860  
 aaagtaaaaa aggtcaatgt gaaaaccctt ttgacctga aaaaggcctt agtatggtcc 1920

347

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&lt;210&gt; 338

&lt;211&gt; 353

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 338

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 20          25          30
Val Leu Cys Val Gly Thr Phe Phe Cys Leu Phe Ile Phe Phe Ser Asn
 35          40          45
Ser Leu Val Ile Ala Ala Val Ile Lys Asn Arg Lys Phe His Phe Pro
 50          55          60
Phe Tyr Tyr Leu Leu Ala Asn Leu Ala Ala Asp Phe Phe Ala Gly
 65          70          75          80
Ile Ala Tyr Val Phe Leu Met Phe Asn Thr Gly Pro Val Ser Lys Thr
 85          90          95
Leu Thr Val Asn Arg Trp Phe Leu Arg Gln Gly Leu Leu Asp Ser Ser
100          105          110
Leu Thr Ala Ser Leu Thr Asn Leu Leu Val Ile Ala Val Glu Arg His
115          120          125
Met Ser Ile Met Arg Met Arg Val His Ser Asn Leu Thr Lys Lys Arg
130          135          140
Val Thr Leu Leu Ile Leu Leu Val Trp Ala Ile Ala Ile Phe Met Gly
145          150          155          160
Ala Val Pro Thr Leu Gly Trp Asn Cys Leu Cys Asn Ile Ser Ala Cys

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Val	Ser	Asn	Leu	Met	Ala	Phe	Leu	Ile	Met	Val	Val	Val	Tyr	Leu	Arg																																	
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225																230																235																240
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Tyr	Ile	Glu	Asp	Ser	Ile	Ser	Gln	Gly	Ala	Val	Cys	Asn	Lys	Ser	Thr																																	
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Ser																																																

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<211> 3320
<212> DNA
<213> Homo sapiens
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349

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aggtgtggcc aggtgtctcc tcgaggaggc tgggagctgg ccgactgcaa agccagact 3000
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aaaaaaaaa aaaaaaaaaa 3320

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&lt;210&gt; 340

&lt;211&gt; 784

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 340

```

Met Gly Ser Thr Asp Ser Lys Leu Asn Phe Arg Lys Ala Val Ile Gln
 1           5           10           15
Leu Thr Thr Lys Thr Gln Pro Val Glu Ala Thr Asp Asp Ala Phe Trp
      20           25           30
Asp Gln Phe Trp Ala Asp Thr Ala Thr Ser Val Gln Asp Val Phe Ala
      35           40           45
Leu Val Pro Ala Ala Glu Ile Arg Ala Val Arg Glu Glu Ser Pro Ser
      50           55           60
Asn Leu Ala Thr Leu Cys Tyr Lys Ala Val Glu Lys Leu Val Gln Gly
65           70           75           80
Ala Glu Ser Gly Cys His Ser Glu Lys Glu Lys Gln Ile Val Leu Asn
      85           90           95
Cys Ser Arg Leu Leu Thr Arg Val Leu Pro Tyr Ile Phe Glu Asp Pro
      100          105          110
Asp Trp Arg Gly Phe Phe Trp Ser Thr Val Pro Gly Ala Gly Arg Gly
      115          120          125
Gly Gln Gly Glu Glu Asp Asp Glu His Ala Arg Pro Leu Ala Glu Ser
      130          135          140
Leu Leu Leu Ala Ile Ala Asp Leu Leu Phe Cys Pro Asp Thr Gln Ser
145          150          155          160

```

350

His	Arg	Arg	Ser	Thr	Val	Asp	Ser	Ala	Glu	Asp	Val	His	Ser	Leu	Asp
				165						170				175	
Ser	Cys	Glu	Tyr	Ile	Trp	Glu	Ala	Gly	Val	Gly	Phe	Ala	His	Ser	Pro
			180					185					190		
Gln	Pro	Asn	Tyr	Ile	His	Asp	Met	Asn	Arg	Met	Glu	Leu	Leu	Lys	Leu
		195					200					205			
Leu	Leu	Thr	Cys	Phe	Ser	Glu	Ala	Met	Tyr	Leu	Pro	Pro	Ala	Pro	Glu
		210				215					220				
Ser	Gly	Ser	Thr	Asn	Pro	Trp	Val	Gln	Phe	Phe	Cys	Ser	Thr	Glu	Asn
225				230						235				240	
Arg	His	Ala	Leu	Pro	Leu	Phe	Thr	Ser	Leu	Leu	Asn	Thr	Val	Cys	Ala
			245						250					255	
Tyr	Asp	Pro	Val	Gly	Tyr	Gly	Ile	Pro	Tyr	Asn	His	Leu	Leu	Phe	Ser
			260				265						270		
Asp	Tyr	Arg	Glu	Pro	Leu	Val	Glu	Ala	Gln	Val	Leu	Ile	Val	Thr	Leu
		275					280					285			
Asp	His	Asp	Ser	Ala	Ser	Ser	Ala	Ser	Pro	Thr	Val	Asp	Gly	Thr	Thr
		290				295					300				
Thr	Gly	Thr	Ala	Met	Asp	Asp	Ala	Asp	Pro	Pro	Gly	Pro	Glu	Asn	Leu
305				310						315				320	
Phe	Val	Asn	Tyr	Leu	Ser	Arg	Ile	His	Arg	Glu	Glu	Asp	Phe	Gln	Phe
			325						330					335	
Ile	Leu	Lys	Gly	Ile	Ala	Arg	Leu	Leu	Ser	Asn	Pro	Leu	Leu	Gln	Thr
			340						345				350		
Tyr	Leu	Pro	Asn	Ser	Thr	Lys	Lys	Ile	Gln	Phe	His	Gln	Glu	Leu	Leu
		355					360					365			
Val	Leu	Phe	Trp	Lys	Leu	Cys	Asp	Phe	Asn	Lys	Lys	Phe	Leu	Phe	Phe
		370				375					380				
Val	Leu	Lys	Ser	Ser	Asp	Val	Leu	Asp	Ile	Leu	Val	Pro	Ile	Leu	Phe
385				390						395				400	
Phe	Leu	Asn	Asp	Ala	Arg	Ala	Asp	Gln	Ser	Arg	Val	Gly	Leu	Met	His
			405						410					415	
Ile	Gly	Val	Phe	Ile	Leu	Leu	Leu	Ser	Gly	Glu	Arg	Asn	Phe	Gly	
			420					425				430			
Val	Arg	Leu	Asn	Lys	Pro	Tyr	Ser	Ile	Arg	Val	Pro	Met	Asp	Ile	Pro
		435					440					445			
Val	Phe	Thr	Gly	Thr	His	Ala	Asp	Leu	Leu	Ile	Val	Val	Phe	His	Lys
		450				455					460				
Ile	Ile	Thr	Ser	Gly	His	Gln	Arg	Leu	Gln	Pro	Leu	Phe	Asp	Cys	Leu
465				470						475				480	
Leu	Thr	Ile	Val	Val	Asn	Val	Ser	Pro	Tyr	Leu	Lys	Ser	Leu	Ser	Met
			485						490					495	
Val	Thr	Ala	Asn	Lys	Leu	Leu	His	Leu	Leu	Glu	Ala	Phe	Ser	Thr	Thr
			500					505					510		
Trp	Phe	Leu	Phe	Ser	Ala	Ala	Gln	Asn	His	His	Leu	Val	Phe	Phe	Leu
		515					520					525			
Leu	Glu	Val	Phe	Asn	Asn	Ile	Ile	Gln	Tyr	Gln	Phe	Asp	Gly	Asn	Ser
		530				535					540				
Asn	Leu	Val	Tyr	Ala	Ile	Ile	Arg	Lys	Arg	Ser	Ile	Phe	His	Gln	Leu
545				550						555				560	
Ala	Asn	Leu	Pro	Thr	Asp	Pro	Pro	Thr	Ile	His	Lys	Ala	Leu	Gln	Arg
			565						570					575	
Arg	Arg	Arg	Thr	Pro	Glu	Pro	Leu	Ser	Arg	Thr	Gly	Ser	Gln	Glu	Gly
			580					585					590		
Thr	Ser	Met	Glu	Gly	Ser	Arg	Pro	Ala	Ala	Pro	Ala	Glu	Pro	Gly	Thr
		595					600					605			
Leu	Lys	Thr	Ser	Leu	Val	Ala	Thr	Pro	Gly	Ile	Asp	Lys	Leu	Thr	Glu
		610				615					620				

351

Lys Ser Gln Val Ser Glu Asp Gly Thr Leu Arg Ser Leu Glu Pro Glu  
 625 630 635 640  
 Pro Gln Gln Ser Leu Glu Asp Gly Ser Pro Ala Lys Gly Glu Pro Ser  
 645 650 655  
 Gln Ala Trp Arg Glu Gln Arg Arg Pro Ser Thr Ser Ser Ala Ser Gly  
 660 665 670  
 Gln Trp Ser Pro Thr Pro Glu Trp Val Leu Ser Trp Lys Ser Lys Leu  
 675 680 685  
 Pro Leu Gln Thr Ile Met Arg Leu Leu Gln Val Leu Val Pro Gln Val  
 690 695 700  
 Glu Lys Ile Cys Ile Asp Lys Gly Leu Thr Asp Glu Ser Glu Ile Leu  
 705 710 715 720  
 Arg Phe Leu Gln His Gly Thr Leu Val Gly Leu Leu Pro Val Pro His  
 725 730 735  
 Pro Ile Leu Ile Arg Lys Tyr Gln Ala Asn Ser Gly Thr Ala Met Trp  
 740 745 750  
 Phe Arg Thr Tyr Met Trp Gly Val Ile Tyr Leu Arg Asn Val Asp Pro  
 755 760 765  
 Pro Val Trp Tyr Asp Thr Asp Val Lys Leu Phe Glu Ile Gln Arg Val  
 770 775 780

&lt;210&gt; 341

&lt;211&gt; 3307

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 341

gggccgcgga gctggagccg gagctgaagc cggagccggg ttggagtctg ggcgggggccc 60  
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 cggatgatcca gctcaccacc aagacgcagc ccgtggaagc caccgatgat gccttttggg 180  
 accagttctg ggcagacaca gccacctcgg tgcaggatgt gtttgcaactg gtgccggcag 240  
 cagagatccg ggccgtgagg gaagagtcac cctccaactt ggccaccctg tgctacaagg 300  
 ccgttgagaa gctgggtgcag ggagctgaga gtggctgcca ctgggagaag gagaagcaga 360  
 tgcgtctgaa ctgcagccgg ctgctcaccg gcgtgctgcc ctacatcttt gaggaccccg 420  
 actggagggg cttcttcttg tccacagtgc ccggggcagg gcgaggaggg caggggagaag 480  
 aggatgatga gcatgccagg cccctggccg agtccctgct cctggccatt gctgacctgc 540  
 tcttctgccc ggacttcacg gttcagagcc accggaggag cactgtggac tcggcagagg 600  
 acgtccactc cctggacagc tgtgaataca tctgggaggc tgggtgtggc ttcgctcact 660  
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 ccatcatccg caagcgcagc atcttcacc agctggccaa cctgcccacg gaccgccc 1800

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aaaaaaaaa 3307

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&lt;210&gt; 342

&lt;211&gt; 788

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 342

```

Met Gly Ser Thr Asp Ser Lys Leu Asn Phe Arg Lys Ala Val Ile Gln
 1           5           10          15
Leu Thr Thr Lys Thr Gln Pro Val Glu Ala Thr Asp Asp Ala Phe Trp
          20          25          30
Asp Gln Phe Trp Ala Asp Thr Ala Thr Ser Val Gln Asp Val Phe Ala
          35          40          45
Leu Val Pro Ala Ala Glu Ile Arg Ala Val Arg Glu Glu Ser Pro Ser
          50          55          60
Asn Leu Ala Thr Leu Cys Tyr Lys Ala Val Glu Lys Leu Val Gln Gly
65          70          75          80
Ala Glu Ser Gly Cys His Ser Glu Lys Glu Lys Gln Ile Val Leu Asn
          85          90          95
Cys Ser Arg Leu Leu Thr Arg Val Leu Pro Tyr Ile Phe Glu Asp Pro
          100         105         110
Asp Trp Arg Gly Phe Phe Trp Ser Thr Val Pro Gly Ala Gly Arg Gly
          115         120         125
Gly Gln Gly Glu Glu Asp Asp Glu His Ala Arg Pro Leu Ala Glu Ser
          130         135         140
Leu Leu Leu Ala Ile Ala Asp Leu Leu Phe Cys Pro Asp Phe Thr Val
145         150         155         160
Gln Ser His Arg Arg Ser Thr Val Asp Ser Ala Glu Asp Val His Ser
          165         170         175
Leu Asp Ser Cys Glu Tyr Ile Trp Glu Ala Gly Val Gly Phe Ala His
          180         185         190
Ser Pro Gln Pro Asn Tyr Ile His Asp Met Asn Arg Met Glu Leu Leu

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353

195	200	205
Lys Leu Leu Leu Thr Cys Phe Ser Glu Ala Met Tyr Leu Pro Pro Ala		
210	215	220
Pro Glu Ser Gly Ser Thr Asn Pro Trp Val Gln Phe Phe Cys Ser Thr		
225	230	235
Glu Asn Arg His Ala Leu Pro Leu Phe Thr Ser Leu Leu Asn Thr Val		
245	250	255
Cys Ala Tyr Asp Pro Val Gly Tyr Gly Ile Pro Tyr Asn His Leu Leu		
260	265	270
Phe Ser Asp Tyr Arg Glu Pro Leu Val Glu Glu Ala Ala Gln Val Leu		
275	280	285
Ile Val Thr Leu Asp His Asp Ser Ala Ser Ser Ala Ser Pro Thr Val		
290	295	300
Asp Gly Thr Thr Thr Gly Thr Ala Met Asp Asp Ala Asp Pro Pro Gly		
305	310	315
Pro Glu Asn Leu Phe Val Asn Tyr Leu Ser Arg Ile His Arg Glu Glu		
325	330	335
Asp Phe Gln Phe Ile Leu Lys Gly Ile Ala Arg Leu Leu Ser Asn Pro		
340	345	350
Leu Leu Gln Thr Tyr Leu Pro Asn Ser Thr Lys Lys Ile Gln Phe His		
355	360	365
Gln Glu Leu Leu Val Leu Phe Trp Lys Leu Cys Asp Phe Asn Lys Lys		
370	375	380
Phe Leu Phe Phe Val Leu Lys Ser Ser Asp Val Leu Asp Ile Leu Val		
385	390	395
Pro Ile Leu Phe Phe Leu Asn Asp Ala Arg Ala Asp Gln Ser Arg Val		
405	410	415
Gly Leu Met His Ile Gly Val Phe Ile Leu Leu Leu Leu Ser Gly Glu		
420	425	430
Arg Asn Phe Gly Val Arg Leu Asn Lys Pro Tyr Ser Ile Arg Val Pro		
435	440	445
Met Asp Ile Pro Val Phe Thr Gly Thr His Ala Asp Leu Leu Ile Val		
450	455	460
Val Phe His Lys Ile Ile Thr Ser Gly His Gln Arg Leu Gln Pro Leu		
465	470	475
Phe Asp Cys Leu Leu Thr Ile Val Val Asn Val Ser Pro Tyr Leu Lys		
485	490	495
Ser Leu Ser Met Val Thr Ala Asn Lys Leu Leu His Leu Leu Glu Ala		
500	505	510
Phe Ser Thr Trp Phe Leu Phe Ser Ala Ala Gln Asn His His Leu		
515	520	525
Val Phe Phe Leu Leu Glu Val Phe Asn Asn Ile Ile Gln Tyr Gln Phe		
530	535	540
Asp Gly Asn Ser Asn Leu Val Tyr Ala Ile Ile Arg Lys Arg Ser Ile		
545	550	555
Phe His Gln Leu Ala Asn Leu Pro Thr Asp Pro Pro Thr Ile His Lys		
565	570	575
Ala Leu Gln Arg Arg Arg Thr Pro Glu Pro Leu Ser Arg Thr Gly		
580	585	590
Ser Gln Glu Gly Thr Ser Met Glu Gly Ser Arg Pro Ala Ala Pro Ala		
595	600	605
Glu Pro Gly Thr Leu Lys Thr Ser Leu Val Ala Thr Pro Gly Ile Asp		
610	615	620
Lys Leu Thr Glu Lys Ser Gln Val Ser Glu Asp Gly Thr Leu Arg Ser		
625	630	635
Leu Glu Pro Glu Pro Gln Gln Ser Leu Glu Asp Gly Ser Pro Ala Lys		
645	650	655
Gly Glu Pro Ser Gln Ala Trp Arg Glu Gln Arg Arg Pro Ser Thr Ser		

354

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        660                665                670
Ser Ala Ser Gly Gln Trp Ser Pro Thr Pro Glu Trp Val Leu Ser Trp
        675                680                685
Lys Ser Lys Leu Pro Leu Gln Thr Ile Met Arg Leu Leu Gln Val Leu
        690                695                700
Val Pro Gln Val Glu Lys Ile Cys Ile Asp Lys Gly Leu Thr Asp Glu
705                710                715                720
Ser Glu Ile Leu Arg Phe Leu Gln His Gly Thr Leu Val Gly Leu Leu
        725                730                735
Pro Val Pro His Pro Ile Leu Ile Arg Lys Tyr Gln Ala Asn Ser Gly
        740                745                750
Thr Ala Met Trp Phe Arg Thr Tyr Met Trp Gly Val Ile Tyr Leu Arg
        755                760                765
Asn Val Asp Pro Pro Val Trp Tyr Asp Thr Asp Val Lys Leu Phe Glu
770                775                780
Ile Gln Arg Val
785

```

<210> 343  
 <211> 563  
 <212> DNA  
 <213> Homo sapiens

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<400> 343
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ctgcagtaaa agctggagga atgagaattt ccaaaaaaca agaaattggc accttgga 180
gacataccaa aaaaacagga ttcgagaaaa caagtgccat tgcaaatgtt gcaaaaatac 240
agacactgga tgccctgaat gacgcactgg agaagctcaa ctataaattt ccagcaacag 300
tgcacatggc gcatcaaaaa cccacacctg ctctggaaaa ggttggtcca ctgaaaagga 360
tctacattat tcagcagcct cgaaaatgtt aagcctggat ttaaaacaca gccgtctggc 420
cagctgcctc gaatatctga cagcttagca aaaagggcca aagctttcca taggcgtgct 480
gcacttgctt ggtaaatata gcagcttttg tatcttcccc tttgacttta ggtaataaag 540
catccaaact tgtaaaaaaa aaa 563

```

<210> 344  
 <211> 107  
 <212> PRT  
 <213> Homo sapiens

```

<400> 344
Met Ala Asn Glu Val Gln Asp Leu Leu Ser Pro Arg Lys Gly Gly His
  1                5                10                15
Pro Pro Ala Val Lys Ala Gly Gly Met Arg Ile Ser Lys Lys Gln Glu
        20                25                30
Ile Gly Thr Leu Glu Arg His Thr Lys Lys Thr Gly Phe Glu Lys Thr
        35                40                45
Ser Ala Ile Ala Asn Val Ala Lys Ile Gln Thr Leu Asp Ala Leu Asn
50                55                60
Asp Ala Leu Glu Lys Leu Asn Tyr Lys Phe Pro Ala Thr Val His Met
65                70                75                80
Ala His Gln Lys Pro Thr Pro Ala Leu Glu Lys Val Val Pro Leu Lys
        85                90                95
Arg Ile Tyr Ile Ile Gln Gln Pro Arg Lys Cys
100                105

```

355

<210> 345  
 <211> 3733  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(3733)  
 <223> n = A,T,C or G

<400> 345  
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 gaagcgtcca aagagggacg gctgtcagcc ctgcttgact gagaaccac cagctcatcc 120  
 cagacacctc atagcaacct atttatacaa agggggaaag aaacacctga gcagaatgga 180  
 atcattatth ttttcccaag gagaaaaccg gggtaaaggg agggaagcaa ttcaatttgg 240  
 agtccctgtg aatgggcttt cagaaggcaa ttaaagaaat ccactcagag aggacttggg 300  
 gtgaaacttg ggtcctgtgg ttttctgatt gtaagtggaa gcaggctctg cacacgctgt 360  
 tggcaaatgt caggaccagg ttaagtgact ggcagaaaaa cttccagggtg gaacaagcaa 420  
 cccaggttct gctgcaagct tgaaggagcc tggagcggga gaaagctaac ttgaacatga 480  
 cctgttgact ttggcaagtt ctagcaacat gctcctaagg aagcgataca ggacagacc 540  
 atgcagactc cagttcctcc tgctgctcct ccagactgtc acagcccaag ccagcaagca 600  
 gatgttgac cctccccacc acaccctgca ccagactgtc acagcccaag ccagcaagca 660  
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356

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taacttggat tgtctgtttg gccaacatg aaaattaaag agtgtaagca gatgtaatgg 2880
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atttgggggt aag 3733

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&lt;210&gt; 346

&lt;211&gt; 639

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 346

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Met Leu Leu Arg Lys Arg Tyr Arg His Arg Pro Cys Arg Leu Gln Phe
  1             5             10             15
Leu Leu Leu Leu Leu Met Leu Gly Cys Val Leu Met Met Val Ala Met
  20             25             30
Leu His Pro Pro His His Thr Leu His Gln Thr Val Thr Ala Gln Ala
  35             40             45
Ser Lys His Ser Pro Glu Ala Arg Tyr Arg Leu Asp Phe Gly Glu Ser
  50             55             60
Gln Asp Trp Val Leu Glu Ala Glu Asp Glu Gly Glu Glu Tyr Ser Pro
  65             70             75             80
Leu Glu Gly Leu Pro Phe Ile Ser Leu Arg Glu Asp Gln Leu Leu
  85             90             95
Val Ala Val Ala Leu Pro Gln Ala Arg Arg Asn Gln Ser Gln Gly Arg
  100            105            110
Arg Gly Gly Ser Tyr Arg Leu Ile Lys Gln Pro Arg Arg Gln Asp Lys
  115            120            125
Glu Ala Pro Lys Arg Asp Trp Gly Ala Asp Glu Asp Gly Glu Val Ser
  130            135            140
Glu Glu Glu Glu Leu Thr Pro Phe Ser Leu Asp Pro Arg Gly Leu Gln
  145            150            155            160
Glu Ala Leu Ser Ala Arg Ile Pro Leu Gln Arg Ala Leu Pro Glu Val
  165            170            175
Arg His Pro Leu Cys Leu Gln Gln His Pro Gln Asp Ser Leu Pro Thr
  180            185            190
Ala Ser Val Ile Leu Cys Phe His Asp Glu Ala Trp Ser Thr Leu Leu
  195            200            205
Arg Thr Val His Ser Ile Leu Asp Thr Val Pro Arg Ala Phe Leu Lys
  210            215            220
Glu Ile Ile Leu Val Asp Asp Leu Ser Gln Gln Gly Gln Leu Lys Ser
  225            230            235            240
Ala Leu Ser Glu Tyr Val Ala Arg Leu Glu Gly Val Lys Leu Leu Arg
  245            250            255
Ser Asn Lys Arg Leu Gly Ala Ile Arg Ala Arg Met Leu Gly Ala Thr
  260            265            270
Arg Ala Thr Gly Asp Val Leu Val Phe Met Asp Ala His Cys Glu Cys

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357

275	280	285
His Pro Gly Trp Leu Glu Pro Leu Leu Ser Arg Ile Ala Gly Asp Arg		
290	295	300
Ser Arg Val Val Ser Pro Val Ile Asp Val Ile Asp Trp Lys Thr Phe		
305	310	315
Gln Tyr Tyr Pro Ser Lys Asp Leu Gln Arg Gly Val Leu Asp Trp Lys		
325	330	335
Leu Asp Phe His Trp Glu Pro Leu Pro Glu His Val Arg Lys Ala Leu		
340	345	350
Gln Ser Pro Ile Ser Pro Ile Arg Ser Pro Val Val Pro Gly Glu Val		
355	360	365
Val Ala Met Asp Arg His Tyr Phe Gln Asn Thr Gly Ala Tyr Asp Ser		
370	375	380
Leu Met Ser Leu Arg Gly Gly Glu Asn Leu Glu Leu Ser Phe Lys Ala		
385	390	395
Trp Leu Cys Gly Gly Ser Val Glu Ile Leu Pro Cys Ser Arg Val Gly		
405	410	415
His Ile Tyr Gln Asn Gln Asp Ser His Ser Pro Leu Asp Gln Glu Ala		
420	425	430
Thr Leu Arg Asn Arg Val Arg Ile Ala Glu Thr Trp Leu Gly Ser Phe		
435	440	445
Lys Glu Thr Phe Tyr Lys His Ser Pro Glu Ala Phe Ser Leu Ser Lys		
450	455	460
Ala Glu Lys Pro Asp Cys Met Glu Arg Leu Gln Leu Gln Arg Arg Leu		
465	470	475
Gly Cys Arg Thr Phe His Trp Phe Leu Ala Asn Val Tyr Pro Glu Leu		
485	490	495
Tyr Pro Ser Glu Pro Arg Pro Ser Phe Ser Gly Lys Leu His Asn Thr		
500	505	510
Gly Leu Gly Leu Cys Ala Asp Cys Gln Ala Glu Gly Asp Ile Leu Gly		
515	520	525
Cys Pro Met Val Leu Ala Pro Cys Ser Asp Ser Arg Gln Gln Gln Tyr		
530	535	540
Leu Gln His Thr Ser Arg Lys Glu Ile His Phe Gly Ser Pro Gln His		
545	550	555
Leu Cys Phe Ala Val Arg Gln Glu Gln Val Ile Leu Gln Asn Cys Thr		
565	570	575
Glu Glu Gly Leu Ala Ile His Gln Gln His Trp Asp Phe Gln Glu Asn		
580	585	590
Gly Met Ile Val His Ile Leu Ser Gly Lys Cys Met Glu Ala Val Val		
595	600	605
Gln Glu Asn Asn Lys Asp Leu Tyr Leu Arg Pro Cys Asp Gly Lys Ala		
610	615	620
Arg Gln Gln Trp Arg Phe Asp Gln Ile Asn Ala Val Asp Glu Arg		
625	630	635

&lt;210&gt; 347

&lt;211&gt; 1891

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(1891)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 347

358

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tattctggct ggagcaattg cactcatcat tggctttggt atttcaggga gacactccat 180
cacagtcact actgtcgct cagctgggaa cattggggag gatggaatcc tgagctgcac 240
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cagaggcccg acagcagtggt ttgctgatca agtgatagtt ggcaatgcct ctttgcggt 420
gaaaaacgtg caactcacag atgctggcac ctacaaatgt tataatcatca cttctaaagg 480
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ggactataat gccagctcag agaccttgcg gtgtgaggct ccccgatggt tccccagcc 600
cacagtggtc tgggcatccc aagttgacca gggagccaac ttctcggaag tctccaatac 660
cagctttgag ctgaactctg agaatgtgac tgaaagggtt gtgtctgtgc tctacaatgt 720
tacgatcaac aacacatact cctgtatgat tgaaaatgac attgccaaag caacagggga 780
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ctccccatta caactaccca atccgaagtg tcaactgtgt caggactaag aaacctggt 1200
tttgagtaga aaagggcctg gaaagagggg agccaacaaa tctgtctgct tctcacatt 1260
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nttcnaagna gaatgnattw aaaatatacy attttcbaa aaaaaaaaaa aaaaaaaaaa 1860
maaagtacct cggccgcgac cacgctaagg g 1891

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&lt;210&gt; 348

&lt;211&gt; 282

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 348

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Met Ala Ser Leu Gly Gln Ile Leu Phe Trp Ser Ile Ile Ser Ile Ile
1           5           10          15
Ile Ile Leu Ala Gly Ala Ile Ala Leu Ile Ile Gly Phe Gly Ile Ser
20          25          30
Gly Arg His Ser Ile Thr Val Thr Thr Val Ala Ser Ala Gly Asn Ile
35          40          45
Gly Glu Asp Gly Ile Leu Ser Cys Thr Phe Glu Pro Asp Ile Lys Leu
50          55          60
Ser Asp Ile Val Ile Gln Trp Leu Lys Glu Gly Val Leu Gly Leu Val
65          70          75          80
His Glu Phe Lys Glu Gly Lys Asp Glu Leu Ser Glu Gln Asp Glu Met
85          90          95
Phe Arg Gly Arg Thr Ala Val Phe Ala Asp Gln Val Ile Val Gly Asn
100         105         110
Ala Ser Leu Arg Leu Lys Asn Val Gln Leu Thr Asp Ala Gly Thr Tyr
115         120         125
Lys Cys Tyr Ile Ile Thr Ser Lys Gly Lys Gly Asn Ala Asn Leu Glu
130         135         140
Tyr Lys Thr Gly Ala Phe Ser Met Pro Glu Val Asn Val Asp Tyr Asn

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359

145		150		155		160
Ala Ser Ser Glu Thr	Leu Arg Cys Glu	Ala Pro Arg Trp Phe	Pro Gln			
	165	170	175			
Pro Thr Val Val Trp	Ala Ser Gln Val	Asp Gln Gly Ala Asn	Phe Ser			
	180	185	190			
Glu Val Ser Asn Thr	Ser Phe Glu	Leu Asn Ser Glu	Asn Val Thr Met			
	195	200	205			
Lys Val Val Ser Val	Leu Tyr Asn Val	Thr Ile Asn Asn Thr	Tyr Ser			
	210	215	220			
Cys Met Ile Glu Asn	Asp Ile Ala Lys	Ala Thr Gly Asp Ile	Lys Val			
225	230	235	240			
Thr Glu Ser Glu Ile	Lys Arg Arg Ser	His Leu Gln Leu	Leu Asn Ser			
	245	250	255			
Lys Ala Ser Leu Cys	Val Ser Ser Phe	Phe Ala Ile Ser	Trp Ala Leu			
	260	265	270			
Leu Pro Leu Ser Pro	Tyr Leu Met Leu	Lys				
	275	280				

<210> 349  
 <211> 1517  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(1517)  
 <223> n = A,T,C or G

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 ttgggagtc atagctaaagc accaggagct gagcactgcc cgctgtgcct gcctgcaagt 240  
 ctgacatggc tcaggagaaa atggagctgg accttgagcc tgacacatct tatgggggaa 300  
 ccctgaggag atccagcagc gctcccctaa tccatgggct cagtgcactt tcacagggtt 360  
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 caatgcagat aagccaatca tgggatgaga gcttgagcct gagtgcagc gattttgaca 540  
 agccggagaa attatattct cctaagagaa ttgacttcac tccagtttct ccagcacctt 600  
 caccaccag gggattcggg aagatgttcg tgagcagcag tggattgcca ccaagtcag 660  
 ttcccagtc aagacgattt tcaagcagga gaagtcagag tccagtcaag tgcattagac 720  
 ccagtgttct tggctctctt aaaagaaaag gtgaaatgga gacagaaaag cagcccaaga 780  
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 ctcttgcttg agagattttt ttttgcctc tgttgactac atagtttcaa atctctctt 1440  
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 tcaagaccat tattttg 1517

<210> 350

360

<211> 243  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> VARIANT  
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 <223> Xaa = Any Amino Acid

<400> 350  
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 20 25 30  
 Ser Asp Leu Ser Gln Val Phe Gln Pro Tyr Thr Leu Arg Thr Arg Arg  
 35 40 45  
 Asn Ser Thr Thr Ile Met Ser Arg His Ser Leu Glu Glu Gly Leu Asp  
 50 55 60  
 Met Val Asn Arg Glu Thr Ala His Glu Arg Glu Met Gln Thr Ala Met  
 65 70 75 80  
 Gln Ile Ser Gln Ser Trp Asp Glu Ser Leu Ser Leu Ser Asp Ser Asp  
 85 90 95  
 Phe Asp Lys Pro Glu Lys Leu Tyr Ser Pro Lys Arg Ile Asp Phe Thr  
 100 105 110  
 Pro Val Ser Pro Ala Pro Ser Pro Thr Arg Gly Phe Gly Lys Met Phe  
 115 120 125  
 Val Ser Ser Ser Gly Leu Pro Pro Ser Pro Val Pro Ser Pro Arg Arg  
 130 135 140  
 Phe Ser Ser Arg Arg Ser Gln Ser Pro Val Lys Cys Ile Arg Pro Ser  
 145 150 155 160  
 Val Leu Gly Pro Leu Lys Arg Lys Gly Glu Met Glu Thr Glu Ser Gln  
 165 170 175  
 Pro Lys Arg Leu Phe Gln Gly Thr Thr Asn Met Leu Ser Pro Asp Ala  
 180 185 190  
 Ala Gln Leu Ser Asp Leu Ser Ser Cys Ser Asp Ile Leu Asp Gly Ser  
 195 200 205  
 Ser Ser Ser Ser Gly Leu Ser Ser Asp Pro Leu Ala Xaa Xaa Gln Arg  
 210 215 220  
 Tyr Arg Arg Val Ser Ser Ser Met Leu Gln Phe Met Leu Phe Val His  
 225 230 235 240  
 Leu Asp Gly

<210> 351  
 <211> 248  
 <212> PRT  
 <213> Homo sapiens

<400> 351  
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 Gly Gly Thr Leu Arg Arg Ser Ser Ser Ala Pro Leu Ile His Gly Leu  
 20 25 30  
 Ser Asp Leu Ser Gln Val Phe Gln Pro Tyr Thr Leu Arg Thr Arg Arg  
 35 40 45  
 Asn Ser Thr Thr Ile Met Ser Arg His Ser Leu Glu Glu Gly Leu Asp  
 50 55 60

361

Met Val Asn Arg Glu Thr Ala His Glu Arg Glu Met Gln Thr Ala Met  
65 70 75 80  
Gln Ile Ser Gln Ser Trp Asp Glu Ser Leu Ser Leu Ser Asp Ser Asp  
85 90 95  
Phe Asp Lys Pro Glu Lys Leu Tyr Ser Pro Lys Arg Ile Asp Phe Thr  
100 105 110  
Pro Val Ser Pro Ala Pro Ser Pro Thr Arg Gly Phe Gly Lys Met Phe  
115 120 125  
Val Ser Ser Ser Gly Leu Pro Pro Ser Pro Val Pro Ser Pro Arg Arg  
130 135 140  
Phe Ser Ser Arg Arg Ser Gln Ser Pro Val Lys Cys Ile Arg Pro Ser  
145 150 155 160  
Val Leu Gly Pro Leu Lys Arg Lys Gly Glu Met Glu Thr Glu Ser Gln  
165 170 175  
Pro Lys Arg Leu Phe Gln Gly Thr Thr Asn Met Leu Ser Pro Asp Ala  
180 185 190  
Ala Gln Leu Ser Asp Leu Ser Ser Cys Ser Asp Ile Leu Asp Gly Ser  
195 200 205  
Ser Ser Ser Ser Gly Leu Ser Ser Asp Pro Leu Ala Lys Gly Ser Ala  
210 215 220  
Thr Ala Glu Ser Pro Val Ala Cys Ser Asn Ser Cys Ser Ser Phe Ile  
225 230 235 240  
Leu Met Asp Asp Leu Ser Pro Lys  
245

<210> 352  
<211> 1529  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(1529)  
<223> n = A,T,C or G

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gccccttagc ccccgccccc agctgccagt cccagcagc tcagtcctgc agtgagagtc 180  
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gtgattttga caagccggag aaattatatt ctcttaagag aattgacttc actccagttt 600  
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caccaagtcc agttcccagt ocaagacgat tttcaagcag gagaagtcag agtccagtca 720  
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cctcagaccc gctggctaaa ggcagcgcta ccgcagagtc tccagtagca tgctccaatt 960  
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tggcatctct cttctccaaa gttcaatttt gtgagcctag tgaccttact agtatctggt 1200  
tttctgatgc tcatttttga tttagtgtt aaatctcaaa tgctgatttt tgattgctta 1260

362

gaggaatcctt ttttcttagt gcctcaaaaa acacctatctt tgagtctata catttaagaa 1320  
 aggcaactgat gtgtattgcc tttaatgggt ccttttccgc agcaagtgat atgacagatt 1380  
 tgatcagaaa ttctcttgct tgagagattt tttttgtcc tctgttgact acatagtttc 1440  
 aaatctctct ttatttcacg atgatataa aattgctttt aattatatna aattttattt 1500  
 tctggatcag cttcaagacc attattttg 1529

&lt;210&gt; 353

&lt;211&gt; 252

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 353

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Asn	Ser	Thr	Thr	Ile	Met	Ser	Arg	His	Ser	Leu	Val	Ser	Ile	Glu	Glu
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Thr	Glu	Ser	Gln	Pro	Lys	Arg	Leu	Phe	Gln	Gly	Thr	Thr	Asn	Met	Leu
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Ser	Pro	Asp	Ala	Ala	Gln	Leu	Ser	Asp	Leu	Ser	Ser	Cys	Ser	Asp	Ile
		195					200						205		
Leu	Asp	Gly	Ser	Ser	Ser	Ser	Ser	Gly	Leu	Ser	Ser	Asp	Pro	Leu	Ala
	210					215						220			
Lys	Gly	Ser	Ala	Thr	Ala	Glu	Ser	Pro	Val	Ala	Cys	Ser	Asn	Ser	Cys
225					230					235				240	
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&lt;210&gt; 354

&lt;211&gt; 1574

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

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&lt;223&gt; n = A,T,C or G

&lt;400&gt; 354

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&lt;210&gt; 355

&lt;211&gt; 267

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 355

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 35          40          45
Asn Ser Thr Thr Ile Met Ser Arg His Ser Leu Leu Leu Ser Ser Ser
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Pro Asn Arg Ile Pro Ser Ser Arg Leu His Gln Ile Lys Arg Glu Glu
 65          70          75          80
Gly Leu Asp Met Val Asn Arg Glu Thr Ala His Glu Arg Glu Met Gln
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Thr Ala Met Gln Ile Ser Gln Ser Trp Asp Glu Ser Leu Ser Leu Ser
100          105          110
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115          120          125
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130          135          140
Lys Met Phe Val Ser Ser Ser Gly Leu Pro Pro Ser Pro Val Pro Ser
145          150          155          160
Pro Arg Arg Phe Ser Ser Arg Arg Ser Gln Ser Pro Val Lys Cys Ile
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364

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225	230	235
Gly Ser Ala Thr Ala Glu Ser Pro Val Ala Cys Ser Asn Ser Cys Ser		
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Ser Phe Ile Leu Met Asp Asp Leu Ser Pro Lys		
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&lt;210&gt; 356

&lt;211&gt; 4458

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 356

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365

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&lt;210&gt; 357

&lt;211&gt; 127

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 357

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 20          25          30
Gly Pro Asp Gln Pro Ala Gly Ser Pro Ala Pro Leu Arg Pro Pro Leu
 35          40          45
Pro Arg Thr Leu Arg Leu Arg Lys Tyr Arg Gly Asn Pro Leu Pro Pro
 50          55          60
Glu Val Arg Gly Ser Leu Pro Glu Gly Ala Pro Trp Ser Arg Ala Pro
 65          70          75          80
Leu Gly Gly His Leu Glu Ala Arg Cys Gly Pro Arg Thr Arg Glu Glu
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366

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 <213> Homo sapiens

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gcaaatyggg gaaagatgaa taaacaaatg aaaaaagat aataaatgaa taagagagat 3420
gaataaacaa atttacatta catgtgatag ttatcatggt atggccttca tgacaagatg 3480
gatgagaata tcaactgatg gatattagcc ttctttcata tctttatatt gaaatatggg 3540
ctttacttca atttgaaggt ctttcatgaa caataaaaaga gagtagaagg actgtctgag 3600
aaggcaggag acatataaaa cagatgactg aaagactgac tagctcctgg aaagggaaac 3660
atTTggaaca tccagagtaa ggcaaatggg cttctaccag cacaacaaag agcctccagg 3720
tggaacatg gaagcagggt atcagagaaa ataaatgtgc aaattcctta tttacaatga 3780
ctcacttaac ccacaaaaca tgtttcactg ctgccttccc cagttgtcgc ttatgtactg 3840
ttgttacctt tcagttacat gcctttgatc ctaaaattct ctacttttgt tgccttatca 3900
gttctttgca atctgcctgt gggtatcagc acttaaagca caattttgaa ggggaaaaaa 3960
atgataatca ccttagtccc aaagaaataa tttgtcaaac tgccttatta gtattaaaaa 4020
cagacacact gaatgaagta gcatgatacg catatctct actcagtatc attggccttt 4080
tatcaaatgg ggaaactata cttttgtatt acatagtttt agaaatcgaa agttagagac 4140
tctttataag taatgtcaag gaacagtaat ttaaaaacaa agttctaaca aatatattgt 4200
ttgcttaatc acaatgcctt caacttgtat ttgaataact aaataggaca tgtcttcctt 4260
ggagctgtgg gcattagtgc agaagcacta cctgcactct aattttcaaa acttaagttt 4320
tattagcaaa tcctcttctc tgtaagactt agctatgaag tggatatatt ttccaaata 4380
tttttctgaa aacatttgtt gttgtaactg cacaataaaa gtccagttgc aattaaaaaa 4440
aaaaaaaaa aaaaaaaaaa 4458

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&lt;210&gt; 360

&lt;211&gt; 583

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 360

368

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ccctgcacc ccgcccggca tagcaccatg cctgcttgtc gcctaggccc gctagccgcc 60
gccctectcc tcagcctgct gctgttcggc ttcaccctag tctcaggcac aggagcagag 120
aagactggcg tgtgccccga gctccaggct gaccagaact gcacgcaaga gtgcgtctcg 180
gacagcgaat gcgcccgaac cctcaagtgc tgcagcgcgg gctgtgccac cttctgcctt 240
ctctgccccca atgataagga gggttcctgc cccaggtga acattaactt tccccagctc 300
ggcctctgtc gggaccagtg ccaggtggac acgcagtgtc ctggccagat gaaatgctgc 360
cgcaatggct gtgggaaggt gtcctgtgtc actcccaatt tctgaggtcc agccaccacc 420
aggctgagca gtgaggagag aaagtttctg cctggccctg catctgggtc cagcccacct 480
gccctcccct ttttcgggac tctgtattcc ctcttggggt gaccacagct tctccctttc 540
ccaaccaata aagtaaccac tttcagcaaa aaaaaaaaaa aaa 583

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&lt;210&gt; 361

&lt;211&gt; 125

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 361

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Met Pro Ala Cys Arg Leu Gly Pro Leu Ala Ala Ala Leu Leu Leu Ser
1          5          10          15
Leu Leu Leu Phe Gly Phe Thr Leu Val Ser Gly Thr Gly Ala Glu Lys
20          25          30
Thr Gly Val Cys Pro Glu Leu Gln Ala Asp Gln Asn Cys Thr Gln Glu
35          40          45
Cys Val Ser Asp Ser Glu Cys Ala Asp Asn Leu Lys Cys Cys Ser Ala
50          55          60
Gly Cys Ala Thr Phe Cys Leu Leu Cys Pro Asn Asp Lys Glu Gly Ser
65          70          75          80
Cys Pro Gln Val Asn Ile Asn Phe Pro Gln Leu Gly Leu Cys Arg Asp
85          90          95
Gln Cys Gln Val Asp Thr Gln Cys Pro Gly Gln Met Lys Cys Cys Arg
100         105         110
Asn Gly Cys Gly Lys Val Ser Cys Val Thr Pro Asn Phe
115         120         125

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&lt;210&gt; 362

&lt;211&gt; 3310

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 362

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ggcggggcgac caaagcgcct gaggaccggc aacatgggtgc ggtcggggaa taaggcagct 60
gttgtgctgt gtatggacgt gggctttacc atgagtaact ccattcctgg tatagaatcc 120
ccatttgaac aagcaaagaa ggtgataacc atgtttgtac agcgacaggt gtttgctgag 180
aacaaggatg agattgcttt agtcctgttt ggtacagatg gcactgacaa tcccctttct 240
ggtggggatc agtatcagaa catcacagtg cacagacatc tgatgctacc agattttgat 300
ttgctggagg acattgaaag caaaatccaa ccagggttctc aacaggctga cttcctggat 360
gcactaatcg tgagcatgga tgtgattcaa catgaaacaa taggaaagaa gtttgagaag 420
aggcatattg aaatattcac tgacctcagc agccgattca gcaaaagtca gctggatatt 480
ataattcata gcttgaagaa atgtgacatc tccctgcaat tcttcttgcc tttctcactt 540
ggcaaggaaag atggaagtgg ggacagagga gatggcccct ttcgcttagg tggccatggg 600
ccttcctttc cactaaaagg aattaccgaa cagcaaaaag aaggtcttga gatagtgaag 660
atggtgatga tatctttaga aggtgaagat gggttggatg aaattttattc attcagttag 720
agtctgagaa aactgtgcgt cttcaagaaa attgagaggc attccattca ctggccctgc 780
cgactgacca ttggctccaa tttgtctata aggtttgcag cctataaatc gattctacag 840
gagagagtta aaaagacttg gacagttgtg gatgcaaaaa ccctaaaaaa agaagatata 900
caaaaagaaa cagttttattg cttaaattgat gatgatgaaa ctgaagtttt aaaagaggat 960
attattcaag ggttccgcta tggaagtgat atagttcctt tctctaaagt ggatgaggaa 1020

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caaatgaaat ataaatcgga ggggaagtgc ttctctgttt tgggattttg taaatcttct 1080
cagggttcaga gaagattctt catgggaaat caagttctaa aggtctttgc agcaagagat 1140
gatgaggcag ctgcagttgc actttcctcc ctgattcatg ctttgatga cttagacatg 1200
gtggccatag ttcgatatgc ttatgacaaa agagctaata ctcaagtcgg cgtggctttt 1260
cctcatatca agcataacta tgagtgttta gtgtatgtgc agctgccttt catggaagac 1320
ttgcggaat acatgttttc atccttgaaa aacagtaaga aatatgctcc caccgagga 1380
cagttgaatg ctggtgatgc tttgattgac tccatgagct tggcaaagaa agatgagaag 1440
acagacaccc ttgaagactt gtttccaacc accaaaatcc caaatcctcg atttcagaga 1500
ttatttcagt gtctgctgca cagagcttta catccccggg agcctctacc cccaattcag 1560
cagcatattt ggaatatgct gaatcctccc gctgaggtga caacaaaag tcagattcct 1620
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ggagtgatga atcctgctga aaacttccgt gttctagtga aacagaagaa ggccagcttt 1860
gaggaagcga gtaaccagct cataaatcac atcgaacagt ttttggtac taatgaaaca 1920
ccgtatttta tgaagagcat agactgcac cgagccttcc gggaagaagc cattaagttt 1980
tcagaagagc agcgttttaa caacttccg aaagcccttc aagagaaagt ggaaattaaa 2040
caattaaatc atttctggga aattgtgtgc caggatggaa ttactctgat caccaaagag 2100
gaagcctctg gaagtctgt cacagctgag gaagccaaaa agtttctggc ccccaaagac 2160
aaaccaagtg gagacacagc agctgtattt gaagaaggtg gtgatgtgga cgatttattg 2220
gacatgatal aggtcgtgga tgtatggga atctaagaga gctgccatcg ctgtgatgct 2280
gggagttcta acaaaacaag ttggatgagg ccattcaagg ggagccaaaa tctcaagaaa 2340
ttcccagcag gttacctgga ggcgatcat ctaattctct gtggaatgaa tacacacata 2400
tatattacaa gggataattt agacccata caagtttata aagagtcatt gttattttct 2460
ggttgggtga ttattttttc tgtggtctta ctgatctttg tatattacat acatgctttg 2520
aagtttctgg aaagtagatc ttttcttgac ctagtatata agtgacagtt gcagcccttg 2580
tgatgtgatc agtctctcat gtggaacctt ggcatgggta ttgatgagtt tcttaaccct 2640
ttccagagtc ctgctttgcc tgatcctcca acagctgtca caacttgtgt tgagcaagca 2700
gtagcatttg ctctctccca acaagcagct ggggttaggaa aacctgggt aaggacggac 2760
tcacttctct ttttagttga ggccttctag ttaccacatt actctgcctc tgtatatagg 2820
tggttttctt taagtggggt gggaagggga gcacaatttc cttcatact cttttaagc 2880
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agtgaacctt tagaaactca aaaactgaga aatttacttc agtagttaga attatatcac 3000
ttcactgttc tctacttga agcctcaaag agagaaagtt tcgttatatt aaaacactta 3060
ggtaactttt cggcttttcc catttctacc taagtcagct tcatctttg tggatggtgt 3120
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ttgccttgag ttccagttcc tctttggtgt acagacttct tggtaaccag tcacctctgt 3240
cttcagcacc ctcataagtc gtcactaata cacagttttg tacatgtaac attaaaggca 3300
taaagtactc                                     3310

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&lt;210&gt; 363

&lt;211&gt; 732

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 363

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Met Val Arg Ser Gly Asn Lys Ala Ala Val Val Leu Cys Met Asp Val
1      5      10      15
Gly Phe Thr Met Ser Asn Ser Ile Pro Gly Ile Glu Ser Pro Phe Glu
20     25     30
Gln Ala Lys Lys Val Ile Thr Met Phe Val Gln Arg Gln Val Phe Ala
35     40     45
Glu Asn Lys Asp Glu Ile Ala Leu Val Leu Phe Gly Thr Asp Gly Thr
50     55     60
Asp Asn Pro Leu Ser Gly Gly Asp Gln Tyr Gln Asn Ile Thr Val His
65     70     75     80
Arg His Leu Met Leu Pro Asp Phe Asp Leu Leu Glu Asp Ile Glu Ser
85     90     95

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370

Lys Ile Gln Pro Gly Ser Gln Gln Ala Asp Phe Leu Asp Ala Leu Ile  
 100 105 110  
 Val Ser Met Asp Val Ile Gln His Glu Thr Ile Gly Lys Lys Phe Glu  
 115 120 125  
 Lys Arg His Ile Glu Ile Phe Thr Asp Leu Ser Ser Arg Phe Ser Lys  
 130 135 140  
 Ser Gln Leu Asp Ile Ile Ile His Ser Leu Lys Lys Cys Asp Ile Ser  
 145 150 155 160  
 Leu Gln Phe Phe Leu Pro Phe Ser Leu Gly Lys Glu Asp Gly Ser Gly  
 165 170 175  
 Asp Arg Gly Asp Gly Pro Phe Arg Leu Gly Gly His Gly Pro Ser Phe  
 180 185 190  
 Pro Leu Lys Gly Ile Thr Glu Gln Gln Lys Glu Gly Leu Glu Ile Val  
 195 200 205  
 Lys Met Val Met Ile Ser Leu Glu Gly Glu Asp Gly Leu Asp Glu Ile  
 210 215 220  
 Tyr Ser Phe Ser Glu Ser Leu Arg Lys Leu Cys Val Phe Lys Lys Ile  
 225 230 235 240  
 Glu Arg His Ser Ile His Trp Pro Cys Arg Leu Thr Ile Gly Ser Asn  
 245 250 255  
 Leu Ser Ile Arg Ile Ala Ala Tyr Lys Ser Ile Leu Gln Glu Arg Val  
 260 265 270  
 Lys Lys Thr Trp Thr Val Val Asp Ala Lys Thr Leu Lys Lys Glu Asp  
 275 280 285  
 Ile Gln Lys Glu Thr Val Tyr Cys Leu Asn Asp Asp Asp Glu Thr Glu  
 290 295 300  
 Val Leu Lys Glu Asp Ile Ile Gln Gly Phe Arg Tyr Gly Ser Asp Ile  
 305 310 315 320  
 Val Pro Phe Ser Lys Val Asp Glu Glu Gln Met Lys Tyr Lys Ser Glu  
 325 330 335  
 Gly Lys Cys Phe Ser Val Leu Gly Phe Cys Lys Ser Ser Gln Val Gln  
 340 345 350  
 Arg Arg Phe Phe Met Gly Asn Gln Val Leu Lys Val Phe Ala Ala Arg  
 355 360 365  
 Asp Asp Glu Ala Ala Ala Val Ala Leu Ser Ser Leu Ile His Ala Leu  
 370 375 380  
 Asp Asp Leu Asp Met Val Ala Ile Val Arg Tyr Ala Tyr Asp Lys Arg  
 385 390 395 400  
 Ala Asn Pro Gln Val Gly Val Ala Phe Pro His Ile Lys His Asn Tyr  
 405 410 415  
 Glu Cys Leu Val Tyr Val Gln Leu Pro Phe Met Glu Asp Leu Arg Gln  
 420 425 430  
 Tyr Met Phe Ser Ser Leu Lys Asn Ser Lys Lys Tyr Ala Pro Thr Glu  
 435 440 445  
 Ala Gln Leu Asn Ala Val Asp Ala Leu Ile Asp Ser Met Ser Leu Ala  
 450 455 460  
 Lys Lys Asp Glu Lys Thr Asp Thr Leu Glu Asp Leu Phe Pro Thr Thr  
 465 470 475 480  
 Lys Ile Pro Asn Pro Arg Phe Gln Arg Leu Phe Gln Cys Leu Leu His  
 485 490 495  
 Arg Ala Leu His Pro Arg Glu Pro Leu Pro Pro Ile Gln Gln His Ile  
 500 505 510  
 Trp Asn Met Leu Asn Pro Pro Ala Glu Val Thr Thr Lys Ser Gln Ile  
 515 520 525  
 Pro Leu Ser Lys Ile Lys Thr Leu Phe Pro Leu Ile Glu Ala Lys Lys  
 530 535 540  
 Lys Asp Gln Val Thr Ala Gln Glu Ile Phe Gln Asp Asn His Glu Asp  
 545 550 555 560

371

Gly	Pro	Thr	Ala	Lys	Lys	Leu	Lys	Thr	Glu	Gln	Gly	Gly	Ala	His	Phe
				565					570					575	
Ser	Val	Ser	Ser	Leu	Ala	Glu	Gly	Ser	Val	Thr	Ser	Val	Gly	Ser	Val
			580					585					590		
Asn	Pro	Ala	Glu	Asn	Phe	Arg	Val	Leu	Val	Lys	Gln	Lys	Lys	Ala	Ser
		595					600					605			
Phe	Glu	Glu	Ala	Ser	Asn	Gln	Leu	Ile	Asn	His	Ile	Glu	Gln	Phe	Leu
	610					615					620				
Asp	Thr	Asn	Glu	Thr	Pro	Tyr	Phe	Met	Lys	Ser	Ile	Asp	Cys	Ile	Arg
625					630					635					640
Ala	Phe	Arg	Glu	Glu	Ala	Ile	Lys	Phe	Ser	Glu	Glu	Gln	Arg	Phe	Asn
				645					650					655	
Asn	Phe	Leu	Lys	Ala	Leu	Gln	Glu	Lys	Val	Glu	Ile	Lys	Gln	Leu	Asn
			660					665					670		
His	Phe	Trp	Glu	Ile	Val	Val	Gln	Asp	Gly	Ile	Thr	Leu	Ile	Thr	Lys
		675					680					685			
Glu	Glu	Ala	Ser	Gly	Ser	Ser	Val	Thr	Ala	Glu	Glu	Ala	Lys	Lys	Phe
	690					695					700				
Leu	Ala	Pro	Lys	Asp	Lys	Pro	Ser	Gly	Asp	Thr	Ala	Ala	Val	Phe	Glu
705					710					715					720
Glu	Gly	Gly	Asp	Val	Asp	Asp	Leu	Leu	Asp	Met	Ile				
				725					730						